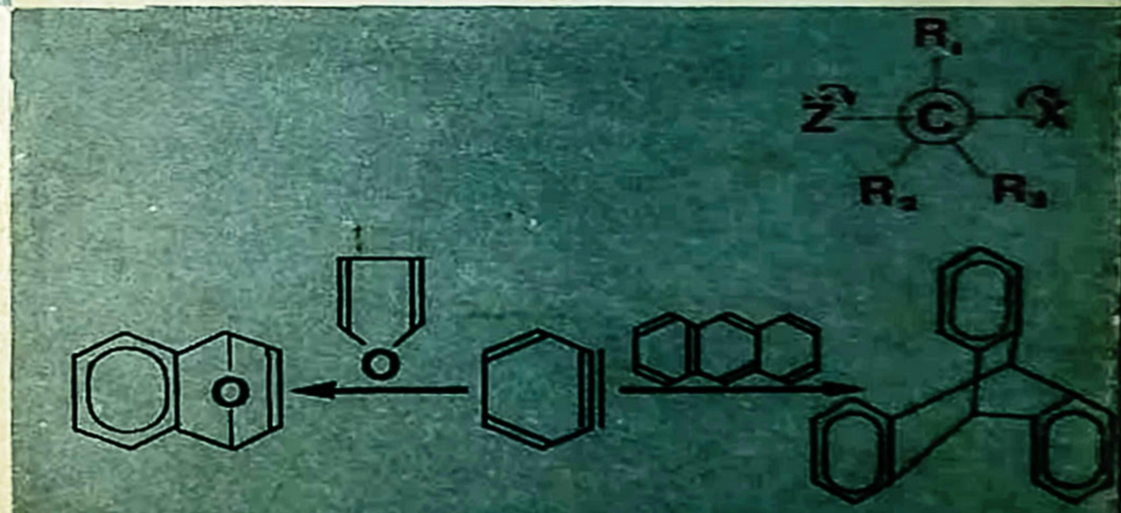
# THEORETICAL PRINCIPLES OF ORGANIC CHEMISTRY

O. Reutov

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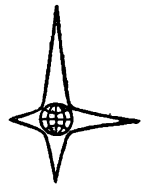
O. REUTOV
Theoretical Principles
of Organic Chemistry



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# ТЕОРЕТИЧЕСКИЕ ПРОБЛЕМЫ ОРГАНИЧЕСКОЙ ХИМИИ

ИЗДАТЕЛЬСТВО МОСКОВСКОГО УНИВЕРСИТЕТА
МОСКВА

# THEORETICAL PRINCIPLES OF ORGANIC CHEMISTRY

by

O. Reutov

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# 1

# THEORY OF CHEMICAL STRUCTURE

## 1-1 BASIC PRINCIPLES OF THE STRUCTURAL THEORY

**Origin and Development of the Theory of Chemical Structure.** By the middle of last century a tremendous amount of experimental data had been accumulated in organic chemistry. However, little attention had been devoted to questions of theory, and the existing theoretical concepts were one-sided, incapable of explaining, not to say predicting, many of the known phenomena and facts. The lag of theory slowed down the development of science.

The mood common among the chemists of the period was picturesquely expressed by Friedrich Wöhler. He wrote: "Organic chemistry nowadays almost drives one mad. To me it appears like a primeval tropical forest, full of the most remarkable things; a dreadful, endless jungle into which one does not dare enter, for there seems to be no way out."

The urgent problems of organic chemistry demanded immediate solution of the basic question: Are organic molecules a disorderly accumulation of atoms, held together by forces of attraction, or are they particles with a definite architecture, with a definite structure, which can be established by investigating the properties of the substance? Gerhardt's theory of types, which was recognized by most chemists with more or less reservations, refused as a matter of principle to go into the question of molecular structure, essentially declaring the latter an unknowable "thing in itself". Meanwhile, by the sixties of last century facts and generalizations had accumulated in organic chemistry, which could serve as a basis for solving the problem of molecular structure. For example, on the basis of experiment it was firmly established by the theory of radicals that in chemical reactions certain groups of atoms are transferred unchanged from the molecule of the initial substance to that of the product. On the other hand, the theory of types made a considerable contribution in the study of most changeable parts of molecules and to a certain degree explained the causes of these changes. Of great importance was Frankland's (1825-1899) discovery of the valence of elements.

Investigating the composition of organometallic compounds, Frankland in 1853 found that each metal forms compounds with a strictly definite number of radicals; this number is the valence of the metal in question. Thus were obtained the following compounds:

| $CH_3Na$ | $(CH_3)_2Hg$ | $(CH_3)_3Al$ | $(CH_3)_4Sn$ |
|---|---|---|---|
| Methylsodium | Dimethylmercury | Trimethylaluminum | Tetramethyltin |

After this discovery it became clear, that atoms may link into molecules only in ratios determined by the valence of the atoms. Kekulé (1829-1896) established, in particular, that carbon is tetravalent (1857).

The discovery of valence led directly to the idea that molecules must have a definite structure. But the question of how to determine molecular structure remained unclear.

Gerhardt (1816-1856), the founder of the theory of types, and his followers considered that molecular structure cannot be determined by studying the reactions of a substance, because the molecule undergoes changes during the reaction. In their opinion, only the past and future states of substances could be established from their chemical properties, but not their present state.* They admitted, however, that in the future physical methods of investigation would make it possible to determine molecular structure. But since these methods were at a low level of development at that time this admission was tantamount to denying the possibility of investigating molecular structure.

A new epoch in organic chemistry ensued with the origin of the theory of chemical structure, the main role in the creation and substantiation of which is due to Butlerov, Kekulé and Couper.

Butlerov challenged the basic agnostic proposition of the theory of types which taught incognizability; he showed that the atoms in the molecule have a definite arrangement, that is, the molecule has a definite chemical structure. Further, Butlerov proved that a chemist can establish molecular structure by studying the chemical properties of a substance, and, conversely, knowing the structure, he can predict many of the properties of the compound. Butlerov did not merely derive this proposition from available experimental

* According to this standpoint, in studying the chemical properties, for instance, of nitrobenzene the following description regarding the nature of the substance would be given: nitrobenzene is a substance, obtained by the action of a nitrating mixture on benzene ("nitrobenzene's past") and is converted to aniline by reduction ("future of nitrobenzene"). Naturally many other definitions of nitrobenzene could be given, for instance, that of a substance obtained from nitrosobenzene by oxidation and convertible to *m*-dinitrobenzene by nitration, and so on. This necessitated describing one and the same substance by many reaction formulas. The question of the structure of a particular molecule was not posed.

data, but predicted on its basis the existence of new substances which were later discovered by him and by other chemists. He became a firm adherent of the materialistic point of view, having shown that a naturalist, while investigating a substance, is capable of learning the inner structure of the molecule.

The basic idea of Butlerov's theory was formulated by him in 1861 in the paper "On the Chemical Structure of Substances". He wrote: "Proceeding from the idea that each *chemical** atom in a substance participates in the formation of the latter and acts here with a definite amount of chemical force (affinity) belonging to it, I call *chemical structure* a distribution of the action of this force, as a result of which chemical atoms, influencing each other directly or indirectly, link into a chemical particle" [1]**.

On the basis of this concept of chemical structure, Butlerov gives a new definition of the nature of substance: "The chemical nature of a complex particle is determined by the nature of its elementary components, their number and by its chemical structure" [2].

This fundamentally new premise (for that time) formed the basis of all later developments of organic chemistry, for it signifies that the structure of a complex substance may be established from its transformations, and its chemical properties (reactivity) may be predicted from its chemical structure. Butlerov points out that all types of reactions may be used for establishing chemical structure: combination (synthesis), decomposition (analysis) and double exchange (substitution). Butlerov was right in considering that chemical structure can be established in this way only if the radicals in the molecule which are not directly involved in the reaction preserve their chemical structure (that is, do not undergo rearrangement).

From the premise of the structural theory that the chemical properties of a compound depend on its structure, ensue Butlerov's views on the importance of structural formulas. He believed that only one structural formula was possible for each compound, and that in the future, when the dependence of the properties on the structure was fully elucidated, the formula of the compound would express all its properties.

With the coming of the theory of chemical structure organic chemistry escaped from the labyrinth of type formulas and was led

* Butlerov spoke of "chemical atoms" rather than just "atoms", meaning by the former the least quantities of elements, contained in molecules.

Butlerov was an adherent of the atomistic theory (at that time still a hypothesis), but because in the middle of the 19th century the existence of physical atoms (the smallest chemically indivisible particles) was considered still unproved, he preferred to use the concept of "chemical atoms". Such prudence was fully warranted at that time.

**See references at end of chapter.

to knowledge of the inner structure of molecules; a theoretical basis was created for understanding of chemical processes and prediction of new approaches to synthesis methods.

The theory of chemical structure made it possible to switch experimental investigations to a directed, purposeful footing. Butlerov himself was a pioneer in this respect. He synthesized the first tertiary alcohol, trimethylcarbinol, according to a previously laid out plan; later Butlerov synthesized other tertiary alcohols on the basis of his structural theory.

A significant success of the theory of chemical structure was the explanation of the phenomenon of *isomerism*, discovered in the first quarter of last century.

At the end of the 18th century the Law of Definite Proportions was established; according to this law every substance has a definite, constant composition. For several decades the reverse of this law was also accepted, i.e., it was thought that only one substance could possess a certain composition. The falsity of the latter proposition was demonstrated by investigations of a number of organic substances. In 1823 Liebig (1803-1873) found that the formula of silver fulminate is equivalent to that of silver isocyanate obtained in 1822 by Wöhler (1800-1882) though it differed sharply in properties from the latter compound.

This notable fact remained unique only for a short time; soon many other substances were found which had the same composition but different properties. At Berzelius' (1799-1848) suggestion this phenomenon was called isomerism (from the Greek for "composed of like parts"). Substances exhibiting isomerism were called isomers. For four decades no satisfactory explanation of the phenomenon of isomerism could be found. Such an explanation became possible after the development of the theory of chemical structure.

As mentioned previously, according to the theory of chemical structure the nature of a substance is determined not only by the character and the number of atoms comprising the molecule but by structure as well. Hence, there may exist substances having the same composition and molecular weight which are, nevertheless, quite different because of different chemical structure. Thus differences in the chemical structure of isomers are a simple and natural explanation of the phenomenon of isomerism.

The problem of isomerism was a serious trial for the young theory of chemical structure and was brilliantly solved with its aid.

An important feature of Butlerov's teaching is that the molecule is not regarded as a mere carcass binding separate atoms into a dead, lifeless construction. Butlerov wrote: "...currently we regard a chemical compound not as something dead, immobile; we accept, on the contrary, that it possesses constant motion enclosed in its

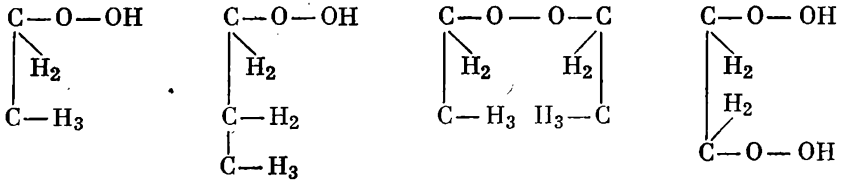
minutest particles, the private mutual relations of which are subject to constant changes, which add up to a certain average result. We may have here constant changes in chemical particles, comprising the mass of substances, but all of it adds up to a certain average condition of the mass itself. In general we always face a condition of a certain mobile equilibrium. From this dynamic point of view of the nature of the chemical compound, and of chemical reactions, we explain clearly such phenomena, which were quite incomprehensible from the previous point of view. By way of example we might mention dissociation or how easily we account for reverse reactions nowadays, etc." [3].

The clear, irrefutable premises of the theory of chemical structure guaranteed its universal acceptance.

In a paper entitled "New Chemical Theory" (1858) Couper discarded the theory of types and expressed a point of view, according to which all the peculiarities of organic substances can be accounted for if only two properties of atoms are taken into consideration: "selective affinity" (linkage of atoms) and "degree of affinity" (valence of atoms) [4].

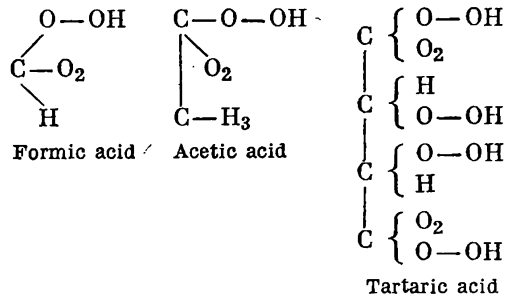
Couper wrote: "From my point of view these two properties are sufficient to explain all that is characteristic of organic chemistry: this I shall prove below.... In a molecule consisting of three, four, five, etc., atoms of carbon and the equivalent quantity of hydrogen, oxygen, etc., the latter may be substituted by other elements, while carbon forms a mutually bound knot. This means that the carbon atoms are linked with each other. Such a property gives carbon, so to speak, a peculiar physiognomy and allows one to understand the hitherto unexplained fact of deposition of carbon atoms in organic compounds."

Having thus arrived at the important concept of chains of carbon atoms, Couper expresses his views in graphic formulas, which, according to his idea, should give a picture of the structure of the compounds. As an example of his formulas, which were the first structural formulas, the following may be given*:



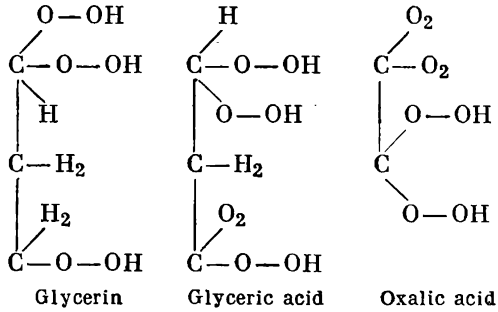

Ethanol *n*-Propanol Ethyl ether Ethyleneglycol

* For correct understanding of Couper's formulas, it should be remembered that Couper considered the atomic weight of oxygen to be 8 (as was generally accepted at the time) and that he always treated oxygen as a double atom with a degree of affinity (valence) equal to two.




These examples show that Couper succeeded in giving the correct structures of these compounds, and of a number of more complex substances, which were rather obscure at that time.

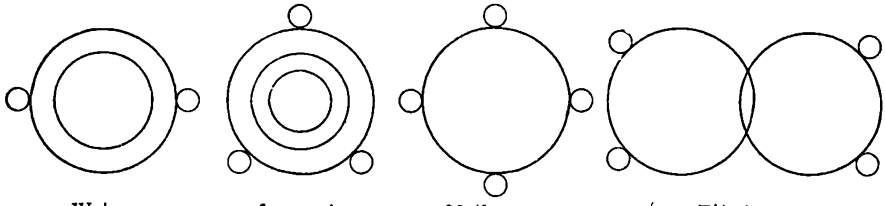
However, all these formulas lacked experimental substantiation. Couper did not even consider the possibility of checking the formulas experimentally. His formulas, obviously, were based on formal interpretation of the concepts of valence and atomic bonds, and partly simply on intuition. Naturally, with such an approach it was impossible to avoid errors. For example, the formulas given by Couper for glycerin, glyceric acid and oxalic acid were incorrect:



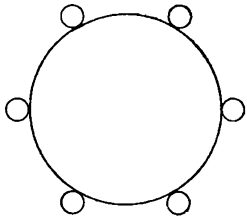

Thus, Couper's views, developed in his talented and interesting work, can hardly be called a harmonious theory.

Another attempt to portray organic compounds by structural formulas was made in 1861 by Loschmidt [5]. In building his formulas Loschmidt regarded atoms as minute material particles subject to the action of forces of attraction and repulsion. When the atoms come close to each other these forces balance and the atoms remain at a certain equilibrium distance from one another. Loschmidt conventionally designated the spheres of action of the atomic forces by circles (for example, carbon and hydrogen atoms by simple circles, oxygen by double, and nitrogen by triple circles).

Loschmidt's formulas had the following appearance:




Not attempting to form any idea of the method of linking of six carbon atoms in the benzene molecule, Loschmidt designated benzene by the following symbol:




Unlike Couper, Loschmidt was sometimes guided by chemical as well as physical considerations in choosing formulas. On the whole, however, Loschmidt's method of deduction of formulas was abstract, and often simply speculative. For instance, though he had no chemical data in his possession, Loschmidt attempted to derive the formulas of such complex substances as indigo, uric acid, etc. Naturally, these formulas were erroneous. Despite the fact that many of the formulas of organic compounds proposed by Loschmidt turned out to be correct, his work remained almost unnoticed by the chemists of the day and had virtually no marked influence on the development of theory of organic chemistry.

A great contribution to the formation of structural theory was made by the famous German chemist Kekulé. He discovered the tetravalence of carbon, proposed the well-known benzene formula, and, what is particularly important, correctly formulated one of the basic problems of organic chemistry of that time.

In his article "Structure and Transformations of Chemical Compounds and Chemical Nature of Carbon" (1858) Kekulé wrote [6]: "I think that at present the main task of chemistry is not the discovery of atomic groups, which owing to certain of their properties may be considered radicals, and the classification of compounds into certain types, which hardly have a meaning outside of a model

formula. On the contrary, I think it is necessary to extend the scope of our speculations to the structure of the radicals; the nature of the radicals and of their compounds should be derived from the nature of the elements." Kekulé considered the point of departure to be valence, and, with regard to organic compounds, primarily the nature of carbon. Kekulé also proposed a number of other correct concepts of atomic bonds, portraying them by graphic formulas.

However, even after 1861 Kekulé did not carry his views out logically. Thus, the second volume of his textbook, published in 1863, was still based on the theory of types.

In his formulas Kekulé strove to express reactivity rather than to indicate structures. He wrote: "The purpose of rational formulas is to give a definite conception of the chemical nature of the compound, of its transformations and of its relation to other bodies.... It must be understood, naturally, that rational formulas are but formulas of transformations and not structural formulas. that they are only a means of expressing the transformation of bodies and the results of comparing different substances with one another and that they should not under any conditions express structure, that is, arrangement of atoms in the compound."

Kekulé considered establishing the true structure of molecules also to be a chemical problem, but in his opinion it could be achieved by a comparative investigation of the physical properties of compounds rather than by studying chemical transformations. Thus, on this question too, he shared Gerhardt's ideas.

Like the other followers of the type theory, Kekulé portrayed a substance by several typical formulas. For example, to convey the properties of acetic acid, known in his time, Kekulé proposed representing it by eight formulas.

Thus, though Kekulé's views were close to new structural concepts, and although Kekulé made a material contribution to the theory of chemical structure, he could not completely shake off the concepts of the theory of types.*

Butlerov rightly considered that the theory of chemical structure would develop with the accumulation of new experimental data. He wrote "...I cannot help noticing that the conclusions depending on the principles of chemical structure agree with the facts in thousands of cases. Of course this theory, like any other, has its faults and imperfections; facts are discovered, which do not correspond strictly to the concept of chemical structure. Understandably, we should wish to multiply such facts; facts which are not explained by existing theories are the most valuable to science, for it is to be

* Concerning the role of Butlerov and Kekulé in the formation of the theory of chemical structure see [7].

expected that the main line of development of science in the near future will be accounting for these facts" [9].

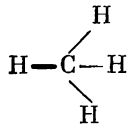
In another place Butlerov pointed out: "He who is vainly convinced of the infallibility of this scientific theory returns in fact from science to blind faith, that is, to that against which he fought." And further: "...blind faith in the infallibility of scientific theories leads to unscientific, unjustifiable skepticism and often prevents one from seeing new real truths, which lie outside the region of pet theories" [10].

In its further development the theory of chemical structure was enriched by a number of new contributions, the most important of which are the stereochemical theory of van't Hoff (1852-1911) and Le Bel (1847-1930) and electronic concepts in organic chemistry.

The theory of chemical structure made possible scientific systematization of the experimental data of organic chemistry, explained its most important laws and provided a key for predicting new facts. The theory of chemical structure became the scientific foundation of present-day organic chemistry.

**Problem of Atomic Interactions Inside Molecules.** Organic chemistry knows a large number of phenomena which without doubt point to the mutual influence of atoms or groups of atoms in the molecules. We must distinguish between the interdependence of directly linked atoms and the interaction of atoms not directly bound. Interdependence of directly bound atoms may be illustrated by silicon tetrachloride, $SiCl_4$, and carbon tetrachloride, $CCl_4$. The chlorine atoms in these compounds differ sharply in reactivity. For instance, chlorine in $SiCl_4$ is readily replaced (substitution reaction) by hydroxyl under the action of water, while with $CCl_4$ under the same conditions this is not the case. The reason for this lies in the difference in influence exerted by silicon and carbon on halogen atoms directly linked with them. In their turn, chlorine atoms have a definite influence on carbon and silicon atoms.

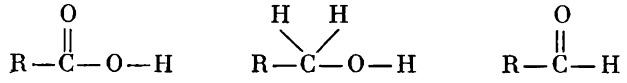
Atoms which are not directly linked also influence each other. Thus the hydrogen in hydrogen cyanide $H - C \equiv N$ differs very noticeably in chemical behaviour from hydrogen in methane



although it is linked directly with carbon in both cases. Here the character of the hydrogen depends on the different influences of the atoms linked to it through carbon (nitrogen atom and hydrogen atoms, respectively).

Naturally, by comparing only two substances it is impossible to trace the influence of atoms upon each other. Thus, when we

compare H — CN and H — $CH_3$, we note only the influence of the nitrogen atom in the first case and that of hydrogen atoms in the second, on the chemical nature of the hydrogen atom with which they are not directly linked. The question of how, on their part, the latter hydrogen atoms influence the nitrogen atom in HCN and the rest of the hydrogen atoms in $CH_4$, remains open. To make the interaction of atoms or groups of atoms more obvious, a large number of compounds must be compared. To show the presence of interaction between the hydroxyl and carbonyl groups in a fatty acid molecule it is necessary to compare at least three compounds: the acid, the primary alcohol and the aldehyde:



Comparing the acid with the primary alcohol, we see that the character of the hydrogen of the hydroxyl group has changed in passing from alcohol to acid (ease of dissociation, ability to be replaced by metals under the action of hydroxides, etc.). This happens due to the exchange, in the primary alcohol, of two hydrogen atoms at the carbon atom bound to the hydroxyl, for an atom of oxygen, and consequently to the influence of the carbonyl group on the hydroxyl group. On the other hand, comparing the aldehyde with the acid, we find that the exchange of an atom of hydrogen in the aldehyde for a hydroxyl group changes the character of the carbonyl group; in the acid the latter becomes less reactive under the influence of the hydroxyl group (it does not give most of the reactions typical of the carbonyl group).

The problem of interaction of atoms was further developed by Butlerov's pupil, Markovnikov (1838-1904), who in 1869 defended his famous dissertation "Data on the Question of Atomic Interactions in Organic Chemistry".

"The question of the influence of elemental atoms on the direction taken by chemical reactions of a complex body is one of the most vital questions of modern chemistry, and is attracting attention of chemists more and more. This question originated naturally when the majority of chemists mastered the theory of chemical structure and it is a direct continuation and further development of this theory," wrote Markovnikov in 1869 [12].

On the basis of numerous experimental data, Markovnikov proposes in his dissertation the following general formulation of the law of atomic interaction: "If the nature of each complex body depends on the nature and number of its component parts, then, in its turn, the nature of each of the elementary parts of which the complex body is composed depends on the properties of the element

with which it is bound and vice versa.... The influence becomes weaker as the distance between them (elementary parts) increases in the general chain of chemical action" [13].

In the process of discovering and establishing the law of interaction of atoms Markovnikov made a number of contributions which became very important for the further theoretical and practical development of organic chemistry. Such are the well-known rule of Markovnikov concerning the order of addition of hydrogen halides and hypochlorous acid to unsymmetrical unsaturated hydrocarbons (page 224) and his idea of the greater ease of substitution of hydrogen on a tertiary than on a secondary or a primary carbon and of hydrogen on a secondary than on a primary carbon atom. Such is his proposition that in the halogenation of fatty acids the halogen replaces the hydrogen on the $\alpha$-carbon first.

The study of atomic interaction, establishment of the laws of this interaction, the discovery of the mechanism which makes it work, now give very interesting material for a deeper understanding of molecular structure and of the reasons for molecular reactivity.

The basic hypotheses and corollaries of the theory of chemical structure may be formulated briefly as follows:

1. Molecules of substances have a definite sequence of chemical linkage between atoms which, according to Butlerov, is called chemical structure.
2. The chemical properties of a substance are determined by the composition and chemical structure of its molecules.
3. Isomerism is due to differences in the chemical structure of substances having the same composition and molecular weight.
4. The structure of a substance can be determined by studying its chemical transformations, because in the majority of cases individual reactions involve changes not in all, but only in some parts of the molecule.
5. The chemical character (reactivity) of the atoms in a molecule depends on the neighbouring atoms. The change in reactivity is largely due to the influence of directly bound atoms. Interactions between atoms not directly bound are generally much weaker.

## 1-2 PRESENT-DAY STATE OF THE THEORY OF CHEMICAL STRUCTURE

### 1-2.1 Electronic Concepts in Organic Chemistry

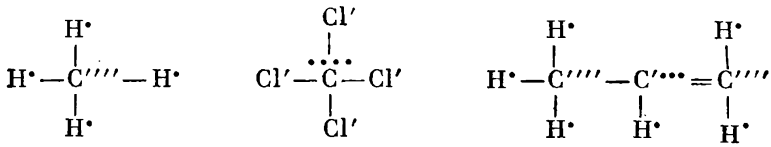
#### Introduction

The discovery of the electron and the appearance of Bohr's theory of atomic structure (1913) promoted the further development of the theory of chemical structure, owing to the introduction of electronic concepts into organic chemistry.

One of the first electronic hypotheses in organic chemistry was suggested in Russia in 1914-1916 by Berkenheim. He based his views on electrostatic concepts. According to Berkenheim's hypothesis carbon fulfills mixed functions, being electropositive in relation to elements like chlorine and electronegative with regard to atoms like hydrogen. The carbon atom fulfills these mixed functions simultaneously with regard to different atoms to which it is linked. According to Berkenheim's hypothesis the chemical bond is formed by a single electron. In inorganic substances this electron may pass from one atom to another, after which the atoms are held together by electrostatic forces alone. In organic molecules the valence electron is not transferred completely from one atom to another but is only displaced towards one of them, for example, from carbon to chlorine, from hydrogen to carbon, etc.*

"We already know that electrons are drawn away from their normal position in the electrically neutral atom to the point of contact with the other atom, reacting with it in such a manner that the electric field of the electron now overlaps this other atom without, however, leaving the original atom," wrote Berkenheim [14].

Formulas of organic compounds were represented by Berkenheim in the following manner**:



Methane | Carbon tetrachloride | Propylene

In methane the carbon atom exhibits fully its negative, and in carbon tetrachloride, its positive valence, being, on the whole, positively charged.

Berkenheim believed that all organic reactions pass through the stage of preliminary dissociation of molecules into ions.

Berkenheim's electronic hypothesis was able to explain certain known facts and laws of organic chemistry because it contained a rational principle. It took into account the electrical negativity of atoms within a molecule, or, in present-day terms, the polarity of individual linkages. However, taking into consideration, as it did, only electrostatic forces, this hypothesis could not be of general value to organic chemistry; attempts to extend it to a number of classes of organic compounds ended in failure. For example, according to Ber-

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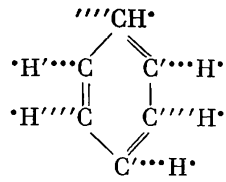
* According to current terminology, the valence electron is displaced towards the more electronegative atom.

** Positive charges are designated by dots, negative charges by strokes.

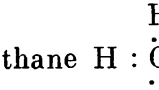
kenheim's hypothesis benzene should have a formula with alternating polarities.



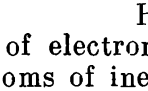
However, at present it has been proved by spectroscopic investigations that the benzene molecule has a centre of symmetry and an axis of symmetry of the sixth order which definitely precludes alternating polarities. Nor could Berkenheim's hypothesis correctly interpret the structure of naphthalene and of many other organic compounds. Inadequate knowledge of the nature of the chemical bond, of valence, rendered other electronic theories and hypotheses developed in the beginning of this century (Frey, Falk and Nelson, Vorländer) unable to serve as a basis for electronic interpretation of a large number of phenomena in organic chemistry.

This is due to the fact that the authors of these hypotheses mechanically extended the concepts of electrostatic heteropolar bonds (which are true for most inorganic compounds) to symmetrical diatomic molecules, such as hydrogen molecules (representing them as $H^+H^-$), and to molecules of hydrocarbons and other organic substances which never exhibited electrolytic dissociation, that is, to linkages which later became known as homopolar.

The idea of electrons being contained simultaneously in the electron shells of two neighbouring atoms became the basis of the so-called octet theory or theory of electron pairs, developed by Kossel and subsequently by Lewis and Langmuir. The basic premise of this theory consists of the following: a bond (single) between atoms is formed not by one, but always by two valence electrons which then become common to the two atoms (Lewis and Langmuir). Representing electrons by dots, the formula of a hydrogen molecule becomes H : H, that of hydrogen chloride H : Cl, and



of methane H : C : H. It is obvious from these formulas that the



atoms of electronegative elements are assumed to be surrounded, like atoms of inert gases, by a shell of eight electrons*, called an octet, for which the theory was named. But, as stated above, the most characteristic premise of this theory is the postulate that the chemical bond (single) is formed by a pair of electrons. Because of this it was suggested to represent a single bond by two dots rather than by a dash.

The octet theory played an important part in clarifying the nature of the chemical bond. It reflected the difference between the ionic and homopolar or covalent bond, characterized more precisely the

* A filled electron shell of the hydrogen atom consists of only two electrons.

valence of certain elements in their compounds, in particular, nitrogen, sulphur and oxygen in onium salts, and introduced the concept of unshared electrons or free electronic pairs. All of this resulted in a deeper understanding of the connection between the chemical structure of organic compounds, their reactivity and their physical properties. The study of the physical properties of organic compounds carried on since the twenties of this century by the most modern physical methods made possible a quantitative description of chemical bonds, i.e., determination of their length, energy, polarity, direction in space, etc.

The weak spot of the octet theory was that it contradicted to some extent the then accepted concepts of atomic structure. According to these concepts, the electrons of the atom are not fixed in space, but revolve about the nucleus at great speeds. Because of this it could not be understood how an electron pair could form a stable definitely directed bond between two atoms.

This contradiction was removed by the quantum theory of the chemical bond, which enabled an explanation, based on the fundamental principles of the electronic theory, of the formation of a covalent bond in the example of the hydrogen molecule (Heitler and London, 1927), and calculation of the energy of formation of this molecule. Later successful calculations were made for other simple molecules.

Physical interpretation of the results of quantum mechanical calculations is very difficult, because the quantum properties of electrons have no analogies in classical physics.

Nevertheless an attempt can be made to picture approximately the scheme of formation of the covalent bond in the hydrogen molecule. As a result of the interaction between the electrons and the nuclei, the density distribution of the electron cloud corresponding to the system of electrons of two atoms of hydrogen changes as the distance between the nuclei diminishes. The character of this change depends substantially on the quantum properties of the electrons, in particular, on the mutual orientation of electronic spins. In the case of antiparallel electronic spins the electron density in the space between the nuclei becomes larger than the sum of the corresponding electron densities of the two isolated atoms. At the same time the energy of the system decreases until a definite distance between the two atoms is reached. This means that the atoms attract each other and a chemical bond is formed. In the case of parallel spins the electron density in the internuclear space of the two atoms diminishes, the energy of the system increases as the atoms approach each other, i.e., the atoms repel each other and, therefore, no bond is formed between them.

Nowadays there is a whole branch of physical chemistry, called quantum chemistry, whose subject is the application of quantum mechanical methods to chemical problems. However, it would be erroneous to think that all questions of structure and reactivity of organic compounds can be reduced to problems of quantum chemistry. Quantum chemistry studies the laws of motion of electrons

and nuclei, that is, laws of a lower form of motion than that studied in chemistry (motion of atoms and molecules), and a higher form of motion cannot be reduced to a lower.

Even in the case of very simple molecules such questions as the reactivity of substances, the mechanism and kinetics of their transformations cannot be studied by the methods of quantum mechanics alone. Therefore, finding appropriate combinations of chemical, quantum-mechanical and physical methods of investigation of organic substances and their reactions is an important problem.

### Types of Chemical Bonding

There is a great variety of chemical bonds differing from one another in various ways. All bonds may be subdivided into several types based on their electronic structure. Given below is the presently accepted classification of chemical bonds.

**Heteropolar (Electrovalent) Bond.** A bond is called heteropolar or electrovalent if its formation involves electrostatic interaction between two atoms or between two groups of atoms.

The most important of this type is the ionic bond, caused by electrostatic attraction of the surplus electrical charges of oppositely charged ions. Metallic atoms, for instance, readily lose their outer electrons, and atoms of nonmetals, on the contrary, tend to gain additional electrons. This may result in the formation of stable cations and anions which retain their electronic structure in the main when they approach each other to form a molecule or a crystal. Crystals of alkali halides contain no separate MeX molecules. The crystals consist of metal cations and chloride anions. The crystal lattice of most halides has the structure shown in Figure 1-1 which is that of sodium chloride.

Strong forces of attraction are at work between each ion and the six ions of opposite sign forming an octahedron around it.* In other words each ion forms ionic bonds with six of its neighbours. These bonds unite all the ions in the crystal into one gigantic "molecule". In such crystals the coordination number of the ions equals six, the coordination number being the number of nearest neighbours around the ion in question.

In caesium chloride, bromide or iodide the crystal lattice has a different structure: all the ions at the corners of the cube are identical and the ions of the opposite sign form a similar system of cubes, the corners of which are in the centres of the cubes of the first system. In this case the coordination number is eight.

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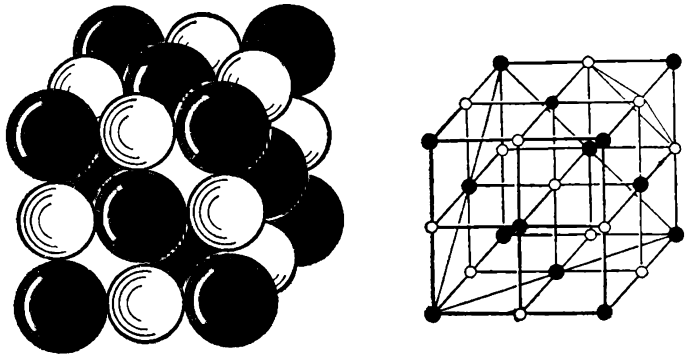
* Naturally, there are also repulsion forces between the like ions though they are not right next to one another.

Ionic molecules are generally represented as follows:

$$Na^+Cl^-;\ K^+Br^-;\ Cs^+Cl^-\ \text{or}\ Na^{\bullet}Cl';\ K^{\bullet}Br',\ \text{etc.}$$

Heteropolar bonds may also be due to attraction between an ion and a molecule possessing a constant or induced dipole, or to attraction between constant dipoles of two molecules. Several bonds of this kind will be examined in greater detail below.



(a) (b)

FIGURE 1-1 Crystal lattice of sodium chloride:
(a) Model of ionic lattice (ions represented by touching spheres). (b) Positions of ion centres

**Homopolar (Covalent) Bond.** A bond is called homopolar or covalent (the latter term is more frequently used at present) if the atoms forming the bond possess close electron affinities.*

The covalent bond in the chemical compounds

$$H{-}H;\ Cl{-}Cl;\ I{-}Br; \qquad \begin{array}{c} H \\ | \\ H{-}C{-}H, \text{ etc.} \\ | \\ H \end{array}$$

is due to the existence of a shared pair of electrons between two linked atoms (electrons are generally designated by dots):

$$H{:}H \quad :\ddot{Cl}{:}\ddot{Cl}: \quad :\ddot{I}{:}\ddot{Br}: \qquad \begin{array}{c} H \\ \cdot\cdot \\ H{:}C{:}H, \text{ etc.} \\ \cdot\cdot \\ H \end{array}$$

* The difference between the heteropolar and the covalent bond may be stated as follows: in heteropolar bonds the forces of attraction are due essentially to simple electrostatic (Coulombic) interaction between the atoms or groups of atoms.

In covalent (homopolar) bonds the forces of attraction are essentially due to "deformation" of the electronic shells of directly interacting atoms.

There are several criteria for differentiating covalent bonds from ionic. An important criterion is polarity, that is, the existence of a constant dipole moment.

The dipole moment of homopolar bonds is not great, and for homopolar bonds of like atoms it is equal or close to zero. On the contrary, ionic bonds possess high polarity. In the extreme case the resultant positive and negative charges are concentrated at the centres of the ions and are at relatively large distances from each other. The dipole moment of an ionic bond equals approximately 9-12 D, because the charge of an electron is $4.8 \times 10^{-10}$ electrostatic units and the length of an ionic bond is 2-3 Å. Experimental data bear out this value (8 D for KCl, 9.07 D for KBr, 10.2 D for CsI).

The most characteristic property of the covalent bond is its saturability. Another important property of the covalent bond distinguishing it from the ionic bond is its invariable steric directionality.* Thus, the angle between the directions of the bonds is 109° 28′ in the covalently linked symmetrical molecules $CH_4$, $CCl_4$ and $C(CH_3)_4$, 120° in $CH_2 = CH_2$ and $CCl_2 = CCl_2$ and so on.

The covalent bonds of oxygen, sulphur, nitrogen, phosphorus, arsenic and certain other elements also have a definite mutual direction in space.

Heteropolar compounds tend to form ionic crystal lattices, the structure of which depends on the ionic dimensions, the magnitude of the forces of repulsion and other factors. A characteristic feature of such lattices is that the bonds between the ion and each of its immediate neighbours are of equal strength. Homopolar compounds in the solid state give molecular crystal lattices, made up of whole molecules which are held in the crystal by the small van der Waals forces. The presence of molecules as discrete units at the nodes of the molecular lattice is due to the property of saturation peculiar to covalent bonds, that is, to the fact that the covalently bound atoms of one molecule may not in addition be linked to the atoms of another molecule**. The differences in structure of ionic and molecular lat-

* In a crystal of ionic structure the bonds between unlike ions also have quite definite space direction. However, often the exchange of one ion in the crystal lattice for another causes a change in the space direction of the bonds (because of the change in the coordination number). For instance, in passing from CsF to CsCl the structure of the crystal lattice changes from octahedral (coordination number 6) to cubic (coordination number 8). Moreover, the space direction of the ionic bonds in a compound may change depending on the conditions of crystallization of the substance. For instance, CsCl generally crystallizes as cubes, but at temperatures above 460° C it forms octahedra. The octahedral crystal lattices of RbCl, RbBr, and RbI change into cubic lattices under a pressure of 5,000 kg/cm².

** Exceptions are molecules of substances capable of forming hydrogen bonds (page 35). Crystal lattices of such substances are made up of molecules linked to each other through hydrogen bonds, in addition to the van der Waals forces.

tices find outward expression in the different physical properties of solid ionic and solid covalent compounds. Thus the energy of sublimation of ionic compounds (transition of a solid body into gaseous molecules) is generally high, for instance, 50-60 kcal/mole for salts of the NaCl type. The energy of sublimation of crystalline covalent compounds is only 10 kcal/mole. Ionic compounds have high melting points, while simple covalent compounds ($H_2$, $Cl_2$, $CH_4$) are gases under ordinary conditions.

The difference between ionic and covalent compounds also becomes evident to a certain degree when they are dissolved in water. Aqueous solutions of ionic compounds conduct electric current owing to the presence of free (more exactly, hydrated) ions. Covalent compounds are often insoluble in water. When covalent compounds do dissolve in water, their solutions contain no ions and, therefore, fail to conduct electricity. However, this criterion should be applied with care. Thus, the hydrogen chloride molecule is covalent, but in water it separates into ions because of the great affinity of water for protons (180 kcal); this is a case of chemical reaction rather than simple solution:

$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

Another criterion of the covalent or ionic nature of a bond may be its energy.

If the energy of the covalent bond $A - B$ is assumed to be equal to the sum of the energies of the $A - A$ and $B - B$ bonds divided by two

$$E_{AB} = 1/2E_{AA} + 1/2E_{BB},$$

the calculated bond energies of covalently linked compounds are in good agreement with those found experimentally. For instance, the energies calculated for the molecules $Br_2$, $Cl_2$, ICl, IBr, NaK are (in kcal) 51, 46, 40 and 14.5 respectively, and the corresponding experimental values are 52, 49, 42 and 14.5. In the case of ionic bonds the bond energies calculated in this way differ sharply from those determined experimentally. Thus, the calculated bond energy of the NaCl molecule is 37 kcal/mole while the experimental value is 98 kcal.

As is the case with any classification in general, the classification of chemical bonds includes many intermediate forms between the ionic and covalent bonds*. However, the existence of qualitative differences in electronic structure between typically ionic and typically covalent bonds as well as of certain typical differences in the

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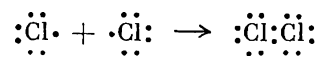
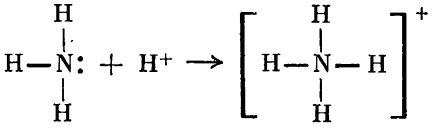
* Hence, it is useful to subdivide covalent bonds into (a) *polar* bonds (with dipole moments $\mu = 1$-2 D) and (b) *homopolar* bonds ($\mu \sim 0$).

properties of ionically and covalently linked compounds confirm the correctness and the legitimacy of such a classification.

Most frequently the covalent bond is formed by sharing of the electrons that originally belonged to the two separate atoms:

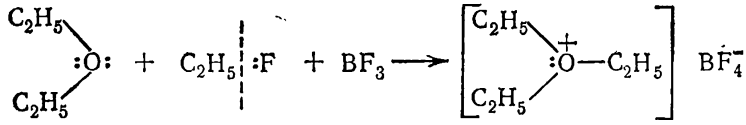


However, another mechanism is possible for the formation of a covalent bond, and this one plays a particularly important part in the chemistry of complex compounds. Thus, the addition of a proton to ammonia results in ammonium ion; the newly formed N — H bond is covalent and is in no way different from the three other bonds present in the original ammonia molecule. The fourth N — H bond could have formed only from the unshared, or free electron pair of the ammonia nitrogen:

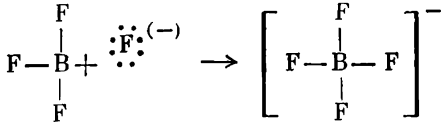


The newly formed covalent N — H bond differs in nothing but origin from the other three bonds.

Similarly, in the reaction between ethyl fluoride, boron trifluoride and ether, the free electron pair of the oxygen forms a covalent bond O — $C_2H_5$ in the triethyloxonium ion:



In the reaction between boron trifluoride and a fluoride anion the fourth covalent bond B — F is formed in the $BF_4^-$ anion through the unshared electron pair of the fluoride ion:

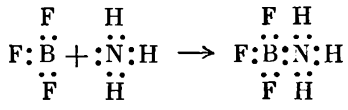


and here also, the newly formed covalent B — F bond is in no way different from the three others, as was the case with the symmetrical ammonium cation.

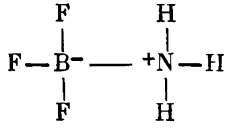
At Lewis and Sedgwick's suggestion a *covalent* bond which forms from an electron pair of only one of the reacting particles is called a *coordinate* bond (also semipolar, donor-acceptor bond). The atom

or ion, which yields the electron pair for the formation of the bond, is known as the donor (the nitrogen atom in the first reaction, the oxygen atom in the second, and the fluoride anion in the third). The atom or ion with an unfilled outer electronic shell, which shares a foreign electron pair is called the acceptor (the proton in the first eaction, the ethyl cation in the second, and the boron atom in the third)*.

A coordinate bond may form through the addition of two molecules, e.g.:



As the B — N bond is formed through sharing of an electron pair, which belonged originally to nitrogen, a simple arithmetical calculation shows that the nitrogen atom acquires a positive, and the boron atom a negative charge (so-called effective charges). Therefore the compound formed when $BF_3$ combines with $NH_3$ may also be represented in the following manner:



This representation of the compound of $BF_3$ with $NH_3$ makes it evident that the coordinate bond B — N may also be called semipolar (or half-polar) because it is shown to be a combination, as it were, of a covalent and an electrovalent bond.

The coordinate bond formed through addition of the above two molecules (in contrast to the case of symmetrical $NH_4^+$ and $BF_4^-$), differs somewhat from other covalent bonds because the resulting molecule is not quite symmetrical. For instance, the dipole moment of this molecule is rather high (2.4-3.5 D). For this reason the graphic representation of coordinate bonds often differs from that used for other types of covalent bonds. For instance, the compound of $BF_3$

---

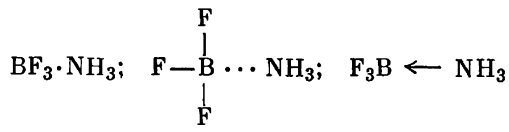
* All chemical reagents may be divided into three groups. Reagents forming a new bond with an electron pair of the substance reacting with them are called *electrophilic* or *electron-acceptor* (less frequently cationoid).

Reagents forming a new bond through their own unshared electron pair are called *nucleophilic* or *electron-donor* (less frequently anionoid).

In the above reactions $H^+$, $C_2H_5^+$ and $BF_3$ are electrophilic, and $NH_3$, $(C_2H_5)_2O$ and $F^-$, nucleophilic reagents.

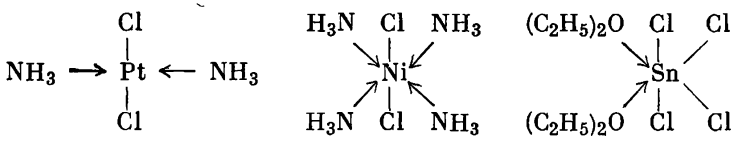
Reagents having an odd (unpaired) electron are called *radicals*.

with $NH_3$ may be also written in the following way:



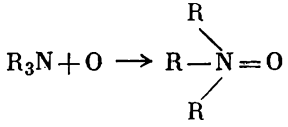
The last method of representation reflects the mechanism of formation of the coordinate bond (the nitrogen atom makes an electron pair available for the formation of the bond).

The chemistry of complex compounds provides numerous examples of coordinate bonds. Such are the complexes:

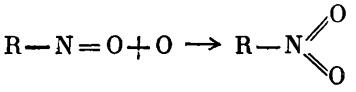


and many others.*

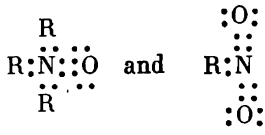
Examples of semipolar linkages of importance to organic chemistry are the oxygen-nitrogen bonds in amine oxides and nitro compounds. To establish the structure of these substances, let us consider two chemical eactions, using, to begin with, the ordinary, non-electronic structural formulas. One of them is the oxidation of a tertiary amine by hydrogen peroxide into amine oxide.



The second is the oxidation of nitroso compounds to nitro compounds



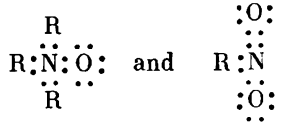
If we now represent the electronic structure of the resulting compounds by substituting electron pairs for valence dashes



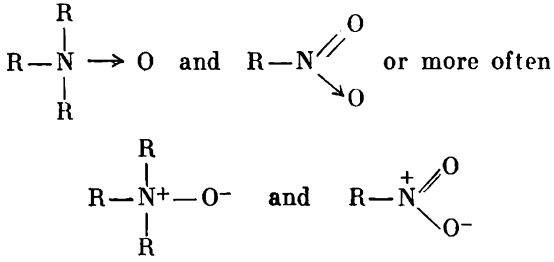
* It should not, however, be thought that the bonds in complex compounds are always coordinate bonds. Many crystal hydrates form as a result of electrostatic attraction between the central cation of the metal salt and the dipole of the water molecule (ion-dipole bond).

it becomes evident that the nitrogen atom in each of these compounds is surrounded not by eight, but by ten electrons and, therefore, the electronic and the corresponding classical structural formulas shown above are incorrect from the standpoint of the octet theory.

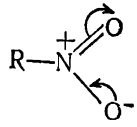
To make the electronic formulas comply with the octet rule they must be rewritten as follows:



A simple count of the electrons convinces us that in the amine oxide the nitrogen is positively charged, and oxygen is negatively charged; in the nitro compound nitrogen is positively charged, and one of the oxygen atoms negatively charged. Generally such formulas are depicted in abbreviated form as follows:



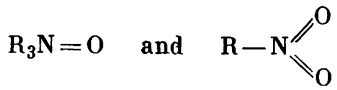
In the above formula of the nitro compound the oxygen-nitrogen bonds are not equivalent. Actually, physical and chemical investigations show these bonds to be fully equal, and, therefore, the electron pair responsible for the negative charge is not totally concentrated on a particular oxygen atom, but is displaced somewhat toward the nitrogen, while one of the electron pairs ($\pi$-electron pair) of the double bond is simultaneously displaced from the nitrogen towards the other oxygen atom. These shifts are limited by the conditions that each of the three atoms under consideration must have an outer electron shell with a charge equal to the charge of eight electrons, and that both N—O bonds must have the same electron density. All these conditions concerning the electronic structure of the nitro group are usually represented as follows:



The curved arrows show the directions of electron shifts, and the unsymmetrical formula of the nitro group derived on the basis of the octet rule only is thus corrected.

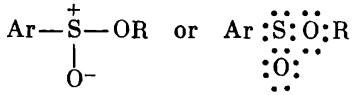
It should be noted that all these precise formulas of amino oxides and nitro compounds are used only when considering the structure of these substances and their reactivities in relation to the fine features of their structure. In all

other cases for simplicity the ordinary structural formulas

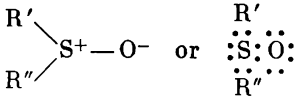


are used, their shortcomings and advantages being clearly understood.

Other examples of compounds having semipolar bonds are esters of sulphinic acids:

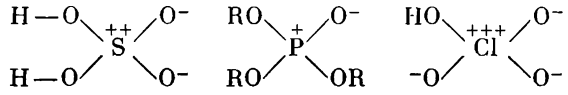


and sulphoxides:

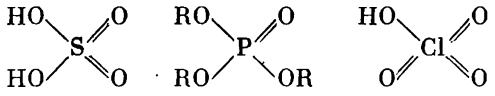


Sulphinic acids esters and unsymmetrical sulphoxides may be divided into optical antipodes. This is in full agreement with the hypothesis that these compounds contain semipolar bonds, because only in such a case has the sulphur atom a free electron pair, the cloud of which has a quite definite direction in space which plays the part of a fourth substituent, differing from the other three; this is what causes optical isomerism, similar to that observed in compounds with asymmetric carbon atoms, in esters of sulphinic acids and in unsymmetrical sulphoxides.

The question whether semipolar bonds exist in the higher oxides and oxygen acids of sulphur, phosphorus, and the halogens, such as



or whether such compounds contain ordinary double bonds



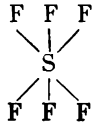
has not found its final solution as yet.*

An argument against the presence of semipolar bonds in such molecules is the fact that the length of these bonds approaches that of ordinary double bonds, while the length of semipolar bonds is

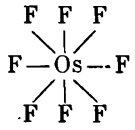
* It is quite evident that the second electron pair (*p* electrons) of each double bond of the central atom with oxygen is shifted considerably toward the latter. The only question that remains unsolved is whether this electron pair belongs entirely to the oxygen or is partly shared by the central atom (S, P or Cl) as well. This alternative is reflected by the two types of formulas given.

close to that of single bonds; the dipole moments of these compounds are much smaller than those calculated for semipolar bonds; the bonds of sulphur, phosphorus and chlorine with oxygen in the above compounds are chemically more stable than typical semipolar bonds.

The existence of semipolar bonds follows from the necessity to conform to the octet rule. However, apparently, for the elements of the third and higher periods of Mendeleyev's periodic table the octet rule need not be fulfilled. Thus, for instance, sulphur in the compound $SF_6$ is hexacovalent:

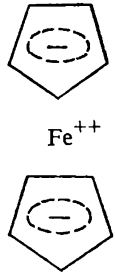



This is confirmed by the great stability of $SF_6$ to chemical reagents (it is not hydrolyzed by strong alkalies on heating). Silicon is hexacovalent in silicofluorides of the type $Na_2SiF_6$; osmium is octacovalent in octafluoroosmium




In the dicyclopentadienyliron (ferrocene) molecule all 6 $\pi$ electrons of each cyclopentadienyl ring (in the form of a $C_5H_5^-$ anion) form approximately octahedrally directed coordination covalent bonds with the free $d^2sp^3$ orbitals of the metal ion $Me^{2+}$. A stable 36-electron shell of a noble gas (krypton) forms around the iron atom and this is responsible for the high stability of the compound.

Such bonds exist in the molecules of all the cyclopentadienyl and benzene derivatives of other transition metals*.



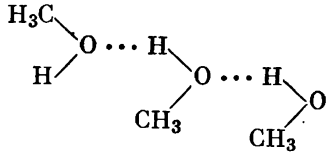

* These concepts of the nature of bonds in compounds of the ferrocene (metallocene) type were developed by E. O. Fischer, et al [15-22]. Other workers, who approached the electronic structure of ferrocene from the standpoint of molecular orbital theory, consider that only part of the $\pi$ electrons of the cyclopentadienyl rings participate in the formation of bonds with iron [23-26].

The metal atoms in the molecules of these substances (metallocenes) are in the same state as the iron atom in the hexacyanoferrate ion.

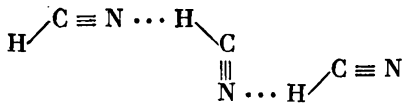
**The Hydrogen Bond.** Besides different heteropolar and homopolar bonds there exists still another special type of bond, which has attracted more and more attention of chemists in the last two decades. This is the so-called hydrogen bond. It was found that hydrogen can form bonds between two electronegative atoms (F, O, N, rarer Cl and S). The hydrogen atom linked with a carbon atom in compounds of the type $HCX_3$, where X is an electronegative atom or group (for example, in HCN, fluorinated hydrocarbons) is also capable of forming a hydrogen bond.

Although at present the nature of the hydrogen bond is not fully known, a definite idea of it may be given.

A hydrogen bond forms between electronegative atoms, of which at least one possesses a free electron pair, for example:



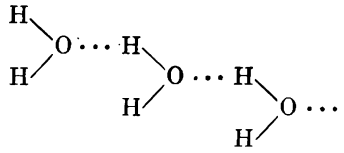
Methanol



Hydrocyanic acid

(hydrogen bonds are designated by three dots).

Thus, the hydrogen bond is evidently mainly electrostatic in nature; it forms as a result of attraction of a covalently linked proton by the unshared electrons of an atom of another molecule. The proton is not equidistant from the two atoms linked to it (even if they are the same) but is nearer the atom with which it is covalently bonded. Thus in the case of water

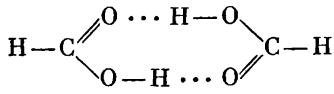


one of the O — H distances is 0.99 Å, and the other 1.76 Å.

The question of whether the hydrogen is in a fixed position or vibrates between two positions of equilibrium is still rather obscure in the general case, although investigation of quinhydrone by the tracer atom method indicates that the hydrogen of the hydrogen bond in this compound is in a fixed position [14].

The energy of the hydrogen bond is small, being of the order of 5-10 kcal/mole, while the energy of the covalent O — H bond is 109 kcal/mole and that of the H — F bond 148 kcal/mole. When ice melts, about 15% of all the hydrogen bonds are broken, and

when water is heated to 40°, about half of the hydrogen bonds are broken. Water vapours contain practically no hydrogen bonds. When alcohols are melted practically no hydrogen bonds are broken; but they are broken completely when alcohols are evaporated. The hydrogen bonds in carboxylic acids do not break even when the latter are evaporated; because of this, formic acid, for example, exists as a dimer even in the vapour phase



However, even in this case the hydrogen bond energy is only 7.0 kcal/mole.

The presence of hydrogen bonds has a substantial influence on the physical properties of compounds. In particular, hydrogen bonds are responsible for the association of water and alcohol molecules and, therefore, for their abnormally high boiling points, as compared, for instance, with hydrogen sulphide and mercaptans. The ability of alcohols, amines, carboxylic acids and amides to dissolve in water is due to the formation of hydrogen bonds with water.

The presence of hydrogen bonds in the molecules of fluorohydrocarbons is indicated by the fact that substitution of fluorine for hydrogen results, as a rule, in lowering of the boiling point. Thus, when compounds of the type $C_nF_{2n+1}H$ are converted to the perfluorocarbons $C_nF_{2n+2}$ having a higher molecular weight, the boiling point is always observed to drop sharply, for example:

| | b.p. |
|---|---|
| $CHF_3$ | −82° |
| $CF_4$ | −130° |
| $CF_3—CHF_2$ | −48.5° |
| $CF_3—CF_3$ | −78° |

Fluorinated derivatives of other types of hydrocarbons, for example, alicyclics, show similar relationships:

| | |
|---|---|
| $C_6H_{11}F$ | +100° |
| $C_6HF_{11}$ | +62° |
| $C_6F_{12}$ | +50° |

Hydrogen bonds show up in infrared and in Raman spectra.

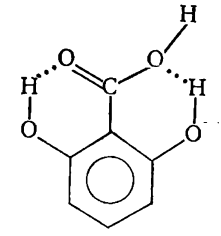
Thus, the infrared spectra of hydroxyl-containing compounds generally display a sharp peak with a maximum absorption in the 3,650-3,590 $cm^{-1}$ range. But if the hydrogen of the OH group participates in an intermolecular hydrogen bond a displaced band (3,400-3,200 $cm^{-1}$) is observed instead of the sharp peak. The strong-

er the hydrogen bond, the greater the shift, a 35 $cm^{-1}$ shift corresponding approximately to 1 kcal/mole.

In the Raman spectra of hydroxyl-containing compounds with intermolecular hydrogen bonds, a broad band appears, displaced toward the lower frequencies instead of the usually observed narrow band at about 3,670 $cm^{-1}$.

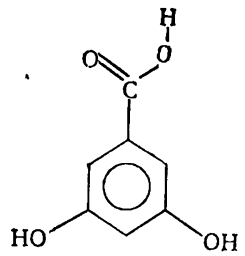
Compounds having intramolecular hydrogen bonds exhibit interesting peculiarities.

2,6-Dihydroxybenzoic ($\gamma$-resorcylic) acid (I) may serve as a striking example. Its dissociation constant is 550 times greater than that of the isomeric 3,5-dihydroxybenzoic ($\alpha$-resorcylic) acid (II), which possesses no intramolecular hydrogen bonds:



$K = 5.0 \times 10^{-2}$ at 25°

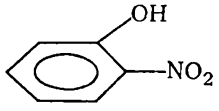
I



$K = 9.1 \times 10^{-5}$ at 25°

II

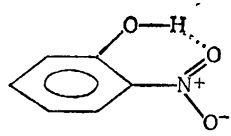
It is interesting to compare the influence of intramolecular hydrogen bonds on the physical properties of compounds, taking *o*- and *p*-nitrophenols (III) and (IV) as examples:



III

IV

Both isomers have hydrogen bonding, but the structure III has intramolecular hydrogen bonding



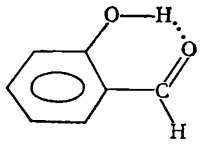
whereas the hydrogen bonds in *p*-nitrophenol are intermolecular.

As a result, the *para*-isomer is associated, while the *ortho*-isomer is not. Besides, the *ortho*-isomer is much more volatile and much more soluble in nonpolar solvents than the *para*-isomer.

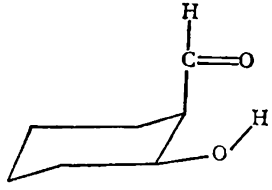
In most of the cases where the presence of an intramolecular hydrogen bond is established, the hydrogen atom is a link of a six-membered planar ring; each of the other five atoms of the ring possesses a single $\pi$ electron.

No intramolecular hydrogen bond forms if the formation of a planar ring is impossible or inhibited.

Thus, there is an intramolecular hydrogen bond in the salicylaldehyde molecule (V), but none in the molecule of its alicyclic analogue (VI):

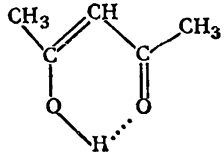


V

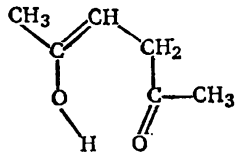


VI

There is an intramolecular hydrogen bond in the enol form of acetoacetic ester, and in the enol form of acetylacetone (VII), but none in the enol form of acetonylacetone (VIII), where its formation would result in a nonplanar seven-membered ring.



VII

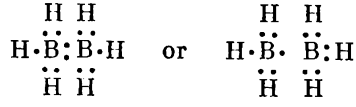


VIII

Hydrogen bonds are widespread, particularly in organic chemistry, where they play an important part; their study should shed additional light on the structure and properties of many organic compounds.

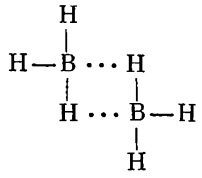
**Single-Electron and Triple-Electron Bonds.** The existence of a single-electron bond must be admitted in the $H_2^+$ ion, in which two protons are linked by a single electron.

It is sometimes thought that single-electron bonds occur in the diborane molecule and one of the following formulas is ascribed to it:



However, the fact that diborane is diamagnetic indicates absence of unpaired electrons, which makes the above structures improbable.

Apparently, it would be more correct to assume, with Nekrasov, the presence of special bonds in diborane, bonds formally resembling hydrogen bonds. However, the mechanism of formation of such bonds is undoubtedly different from that of the formation of hydrogen bonds:



In the $He_2^+$ ion the presence of a triple-electron bond must be assumed.

Bonds between carbon atoms in many aromatic compounds are also essentially formed with the aid of three electrons.

**Covalent and van der Waals Atomic Radii.** When two molecules approach each other without forming a chemical bond, small forces of attraction begin to function. Their origin is due to the mutual deformation of the electron clouds of the two molecules. These forces are called van der Waals or dispersion forces. In the gaseous state they are small because of the relatively large distances between the molecules. However, in the liquid state the molecules are held together by van der Waals forces, and in the crystalline state the same forces keep molecules in their places in the crystal lattice. In many polar substances van der Waals interaction is enhanced by dipole-dipole attraction. However, even in this case molecules cannot approach each other more than to a definite minimum distance, because of the increasing repulsion of electron clouds.

For each atom, which is not part of a molecule, there is a definite characteristic optimum distance from the nucleus, closer than which no other atom can easily approach it. This distance is called the van der Waals radius of the atom or its effective radius of action. The concept of van der Waals radius is applicable also to groups of atoms ($CH_3$, $CH_2$, etc.).

The van der Waals radii of chlorine and bromine were determined in crystallochemical investigations of hexachlorobenzene and hexabromobenzene as half of the shortest distance between the halogen atoms of neighbouring molecules (1.80 Å for Cl and 2.02 Å for Br).

The van der Waals radii of the methyl and methylene groups were found to be equal to a first approximation (about 2.0 Å). They were determined as half of the shortest distance between carbon atoms of the methyl and methylene groups of neighbouring molecules.

Covalent radii are equal to half the bond length of two like atoms. Thus, for instance, the length of a single carbon-carbon bond is

1.54 Å, and the covalent radius of a tetrahedral carbon atom is 0.77 Å.

The covalent and van der Waals radii of some of the elements are listed in Table II (see Appendix).

Covalent and van der Waals radii are now taken into consideration when constructing molecular models, for example, models after Stuart-Brigleb. Such models are excellent visual aids, they give a good idea of the "congestion of space".

### Quantum-Mechanical Concepts of the Structure of the Electron Shell of the Carbon Atom

According to the principles of quantum mechanics the state of the electron in the atom is characterized by four, so called quantum numbers: $n$, $l$, $m$ and $s$, where $n$ is the principal quantum number, mainly determining the energy of the electron; $l$ is the azimuthal (orbital) quantum number, characterizing the moment of momentum of the electron; $m$ is the magnetic quantum number, characterizing the projection of the moment of momentum of the electron on the direction of the outer magnetic field and the orientation of the electron orbital with respect to the outer magnetic field; $s$ is the spin quantum number characterizing a certain moment of momentum of the electron, due to its rotation about its own axis. The quantum numbers $l$, $m$ and $s$ are subject to the following limitations: $l$ cannot be larger than the principal quantum number minus one; $m$ can assume $2l + 1$ different values; $s$ can assume only the values of $+1/2$ and $-1/2$. The structure of the electron shell of a polyelectronic atom always conforms to *Pauli's principle*, according to which no two electrons in a given atom can have the same four quantum numbers.

Possible values of $l$, $m$ and $s$ for a given $n$ are listed below:

| $n$ | $l$ | $m$ | $s$ |
|---|---|---|---|
| 1 | 0 | 0 | $+1/2$; $-1/2$ |
| 2 | 0 | 0 | $+1/2$; $-1/2$ |
| | 1 | $-1$; 0; $+1$ | $+1/2$; $-1/2$ |
| 3 | 0 | 0 | $+1/2$; $-1/2$ |
| | 1 | $-1$; 0; $+1$ | $+1/2$; $-1/2$ |
| | 2 | $-2$; $-1$; 0; $+1$ $+2$ | $+1/2$; $-1/2$ |

From the data given above it is obvious that there can be only two electrons with $n = 1$, eight with $n = 2$, eighteen with $n = 3$ and in general $2n^2$ electrons for any given principal quantum number $n$.

The following conventional designation of electrons is generally accepted: the value of the principal quantum number $n$ is indicated in front with a number (or letter $K$, $L$, $M$, $N$, etc.), and the azimuthal quantum numbers $l$, equal to 0, 1, 2, 3, etc., are designated by the letters $s$, $p$, $d$, $f$, etc., respectively. The number of electrons having the same $n$ and $l$ values (and, therefore, different $m$ and $s$) is designated by a superior index written like the power of a number. Thus, the electron of a hydrogen atom for which $n = 1$ and $l = 0$ is written $1s$, the electron shell of a helium atom, consisting of two electrons with equal $n$ and equal $l$ ($n = 1$, $l = 0$) is written $1s^2$. The electronic shell of lithium consists of three electrons, two of which are the same as in helium ($n = 1$, $l = 0$) and the third is characterized by the principal number $n = 2$ and azimuthal number $l = 0$. Therefore, the electronic shell of lithium is written $1s^22s$.

Following this principle, the structure of the electronic shells of the atoms comprising the first two periods of the periodic system of Mendeleyev may be written as:

| | | | |
|---|---|---|---|
| H . . . . | $1s$ | C . . . . | $1s^22s^22p^2$ |
| He . . . . | $1s^2$ | N . . . . | $1s^22s^22p^3$ |
| Li . . . . | $1s^22s$ | O . . . . | $1s^22s^22p^4$ |
| Be . . . . | $1s^22s^2$ | F . . . . | $1s^22s^22p^5$ |
| B . . . . | $1s^22s^22p$ | Ne . . . . | $1s^22s^22p^6$ |

The distribution of electrons in atoms over energy levels can also be depicted schematically by placing arrows representing electrons in boxes each of which signifies a possible state of these electrons ($1s$, $2s$, $2p$ and so on). The difference in the spins of electrons is represented by different directions of the arrows. According to Pauli's principle there may be only two electrons with antiparallel spins in each box.

According to the quantum theory, the number of unpaired electrons of an atom of a given element is its valence, that is, hydrogen, lithium and fluorine are monovalent, nitrogen is trivalent, oxygen is bivalent; this agrees well with the experimental data. All the electrons of a helium atom and a neon atom are paired, which is in agreement with the inertness of these atoms. In the case of beryllium, boron and carbon the valences obtained in this manner contradict experimental data (the true valences are shown in parentheses).

Of primary interest in organic chemistry is the valence of carbon. In quantum mechanics it is assumed that bivalent carbon when excited changes into tetravalent carbon:

$$1s^22s^22p^2 \longrightarrow 1s^22s2p^3$$

The possibility of this process, which involves a large expenditure of energy (161.5 kcal/mole), is accounted for by the circumstance that such an energy expenditure must be more than compensated by the formation of the two new bonds of tetravalent carbon (186 kcal/mole).

| Atom | State of electron | | | | | Valence |
|---|---|---|---|---|---|---|
| | 1*s* | 2*s* | 2*p* | | | |
| H | ↑ | | | | | 1 |
| He | ↑↓ | | | | | 0 |
| Li | ↑↓ | ↑ | | | | 1 |
| Be | ↑↓ | ↑↓ | | | | 0 (2) |
| B | ↑↓ | ↑↓ | ↑ | | | 1 (3) |
| C | ↑↓ | ↑↓ | ↑ | ↑ | | 2 (4) |
| N | ↑↓ | ↑↓ | ↑ | ↑ | ↑ | 3 |
| O | ↑↓ | ↑↓ | ↑↓ | ↑ | ↑ | 2 |
| F | ↑↓ | ↑↓ | ↑↓ | ↑↓ | ↑ | 1 |
| Ne | ↑↓ | ↑↓ | ↑↓ | ↑↓ | ↑↓ | 0 |

It should be noted that the above idea of the excitation of carbon to convert it from the bivalent to the tetravalent state is of substantial importance only for visuality, because it enables elimination of a seeming contradiction with experimental data. Actually the excitation of carbon from the bivalent to the tetravalent state is an imaginary process. The chemist always has to do with carbon in the mono-, bi- or trivalent states which are conventionally regarded as states of quadrivalent carbon (pages 44-45), even if it is elementary carbon in the form of graphite or diamond.

When considering a carbon atom from the point of view of quantum mechanics at first glance another difficulty arises: the electron orbitals of the *s*- and *p*-electrons have different space configurations—the electron orbital of the *s*-electron being spherical while the *p*-electron orbital has the shape of the solid derived from rotation of the figure eight around its axis (Fig. 1-2, *a*, *b*).

It is easily understood that the four bonds of the excited carbon atom ($1s^2 2s 2p^3$) with other atoms must form through three *p*-electrons and one *s*-electron and, therefore, one of the valence bonds should differ in space configuration from the three others, which is contrary to the experiences of organic chemistry. To eliminate this disparity it was suggested that the orbitals of the three *p*-electrons and the

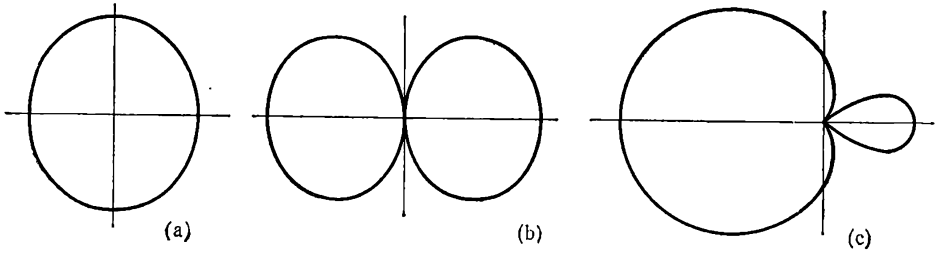



FIGURE 1-2 Shapes of electronic orbitals:
(*a*) *s*-Electron orbital. (*b*) *p*-Electron orbital. (*c*) Hybridized orbital

*s*-electron are "hybridized", forming four identical hybrid electronic orbitals, directed from the centre of a regular tetrahedron to its corners.

Such a hybridization is designated as $sp^3$-hybridization. The directions of the valences under this hybridization are those of the axes of a tetrahedron with an angle of 109°28′.

For comparison, Figure 1-2 shows the shapes of the *s* and *p* electron orbitals, and of the hybridized orbital.

### Electronic Structure of Single and Multiple Carbon-Carbon Bonds

According to current concepts, an electron forms a bond in the direction in which the greatest part of its orbital is located, which results in a maximum overlap of the orbitals of the two binding electrons. Figure 1-3 gives a schematic illustration of the bonds.

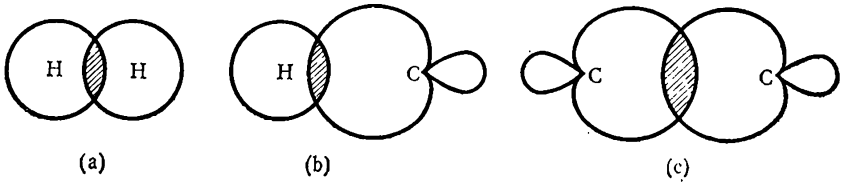
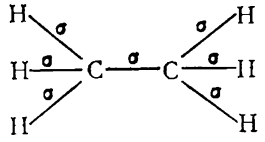



FIGURE 1-3 Single (σ) bonds:
(*a*) A single (σ) bond formed by two *s*-electrons ($H_2$). (*b*) A single (σ) bond formed by an *s*-electron and a hybridized electron (H — C). (*c*) A single (σ) bond formed by two hybridized electrons (C — C). The shaded area is that of the overlap of electronic orbitals

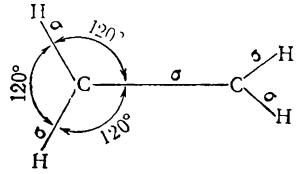
In the case of a single bond (represented by a single valence dash) the maximum overlap is on a straight line joining the two atoms

(Fig. 1-3). Such a simple covalent bond is called a σ bond (sigma bond) and the electrons forming it, σ electrons.

In the ethane molecule, for example, there are seven σ bonds at an angle of 109°28′ to each other. The carbon atoms in such compounds are in the *primary valence state* ($sp^3$ hybridization).



It has been established by physical methods that the five σ bonds in the ethylene molecule are at an angle of 120° to each other and are located in the same plane:



However, with such a distribution of bonds in ethylene each carbon atom retains one unpaired electron. They are no longer able to form a second σ bond between two carbon atoms. Therefore, such

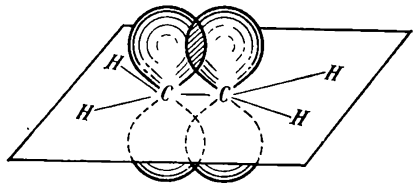


FIGURE 1-4 Scheme of π bonds in an ethylene molecule

unpaired electrons of carbon atoms form a qualitatively different bond by overlapping two electron clouds, the "eights" of which are perpendicular to the plane of the ethylene molecule (Fig. 1-4). Such a bond is called a π bond and the electrons forming it, π electrons. As it is assumed that the three σ bonds of the ethylene carbon atom are formed by hybridized electrons, and the π bond by a "pure" *p* electron (that is, of the four electrons of the carbon atom one *s* electron and only two of the three *p* electrons are hybridized) the electron hybridization taking place in the carbon atom of the ethylene molecule is designated as $sp^2$ hybridization.

The structure of the ethylene molecule may be schematically represented as in Fig. 1-5.

The carbon atoms in an ethylene molecule are in their *second valence state.* Carbon is also in this valence state in aromatic compounds (for more details see Chapter 8).

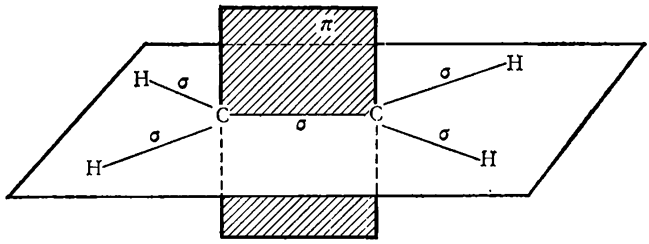



FIGURE 1-5 Diagram of the positions of σ and π bonds in an ethylene molecule. (The π bond plane is shaded, it is perpendicular to the plane of the σ bonds in the molecule.)

In the acetylene molecule carbon is in its *third valence state.* In this molecule all the four atoms are on a common straight line and the angles between the σ bonds are 180° (*sp* hybridization). Two π bonds are arranged in planes at right angles to each other (Fig. 1-6).

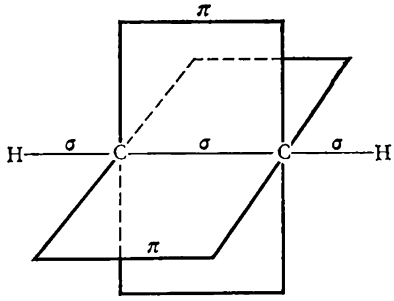



FIGURE 1-6 Diagram of the positions of σ and π bonds in an acetylene molecule

Thus, according to the above models the two carbon bonds in the ethylene molecule and the three in the acetylene molecule (one σ bond and two equivalent π bonds) are not alike in electronic structure. No method has yet been devised which could chemically confirm this difference.

The fact that carbon atoms linked by double bonds readily add only two atoms of hydrogen, halogen, etc., leaving one of the carbon-carbon bonds intact, is easily reconciled with the hypothesis that both carbon-carbon bonds are alike. Indeed, if, say, two atoms of hydrogen are added to one of such identical carbon-carbon bonds,

this may change the character of the remaining carbon-carbon bond and as it is now different from the two initial multiple bonds it may be stronger than either of them. Such an assumption may explain why a double bond readily adds only two, and a triple bond only four equivalents. Non-equivalence of the bonds could be established by physical methods of investigation, the most important of which is determination of the energies of the C — C, C = C and C ≡ C bonds which average 81, 146.5 and 200 kcal/mole, respectively. Apparently, when the second bond forms between carbon atoms the total energy of the bonds between the two atoms does not double but increases only by 61.2 kcal/mole, and this indicates that the π bond is weaker than the σ bond. The increase in the energy between two carbon atoms due to formation of the third bond is still smaller (56.2 kcal/mole)*.

The π bonds are common in organic compounds, being capable of linking not only carbon atoms but also atoms of antimony, arsenic, etc., as well as carbon atoms with atoms of oxygen, nitrogen, sulphur, etc.

When a π bond forms between atoms of different electronegativities, it is polarized, that is, the π electrons forming it are shifted in the direction of the more electronegative atom. In this case the polarization of the π bond is always greater than the polarization of the σ bond binding the same atoms. At the same time during such a polarization π electrons are not transferred wholly from the electron orbital of one atom into that of another.

Consider the polarized π bond in the carbonyl group

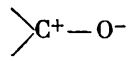
$$\rangle C{=}O$$

It is known from experimental investigations of the dipole moments of a large number of aldehydes and ketones that the dipole moment of the carbonyl group is roughly 2.7 D. It is also known that the dipole moment of the C — O σ bond (from studies of ethers) equals 1.2 D. If the polarization of the π bond were of the same order, then for the carbonyl group one would expect a dipole moment of 1.2 + 1.2 =2.4 D**. However, the dipole moment of the carbon-

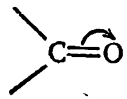
* Such an increase of the bond energies between two atoms shows σ and π bonds to be different only if it is assumed that the energy of the simple C—C bond does not change substantially, when a second bond is formed side by side with it (in the transition C—C → C = C), and then a third. Without this assumption the argumentation of the difference between σ and π bonds with the cited energy of formation values does not make sense. For a quantum mechanical consideration of a double bond as a combination of two equal "bent-bond" linkages see [28].

** More precisely, in this case a still smaller dipole moment than 2.4 D should be expected for the carbonyl group, because the interatomic distances are somewhat smaller in C = O than in C — O.

yl group is actually greater than this figure, and, therefore, the $\pi$ bond is polarized more than the C — O $\sigma$ bond. If, on the other hand, it is assumed that the $\pi$ bond is polarized to the limit and, therefore, the carbonyl group possesses a semipolar bond

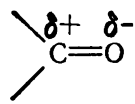


then a dipole moment of the order of 5.7 D should be expected ($\mu = 4.8 \times 10^{-10} \times 1.2 \times 10^{-8} = 5.7$D). Consequently, the $\pi$ bond in the carbonyl group is only partially polarized. This is generally represented as follows:



the bent arrow showing the direction of shift of the $\pi$ electrons, that is, the direction of polarization of the $\pi$ bond.

As a result of such polarization (and also partly of polarization of the $\sigma$ bond) the carbon atom acquires a certain (partial) positive charge and the oxygen atom a certain (also partial) negative charge:



The presence of these charges determines the chemical behaviour of carbonyl compounds in many respects.

### Current Concepts of the Chemical Structure of Molecules and Their Reactivity

Like any other scientific theory, the theory of chemical structure continues to develop as more and more new data accumulate.

During the last two or three decades a great deal of new experimental data was obtained and this required further development of the theory of chemical structure. The majority of new facts concerns the problem of interaction of atoms in molecules. The most important of them are related to the interactions between atoms which are not directly linked, the transfer of interaction down a chain of conjugated bonds, failure of interaction because of steric hindrances, reactivity of aromatic and dienic compounds, and also to the stability of certain free radicals, colour of organic compounds and many other phenomena.

The accumulation of new data in organic chemistry, the application of the latest physical methods of investigation and the use

of quantum-mechanical methods of studying molecular structure resulted in enrichment and development of the concept of chemical structure, which now includes not only the order of chemical linkage of atoms, but the configuration of the molecule as well. With such an understanding of chemical structure the basic premise of the theory of chemical structure, according to which the chemical properties of the molecule are determined by its composition and chemical structure, fully remains in force.

On the basis of a large amount of data and its interpretation from the point of view of the current concepts of atomic structure and of the nature of the chemical bond it became possible to work out several general theses concerning atomic interactions. The most important of these will be considered in this section.

Of great importance is the extensively investigated phenomenon of interactions between atoms directly linked with each other. One of the numerous examples of such interactions is the change in chemical nature of a hydrogen atom depending on what other atom it is linked with*. Thus, if an atom of hydrogen is linked with a carbon atom (C — H bond), it can be removed only with great difficulty as a proton and replaced by a metal when treated with alkali metals; when treated with caustic alkalies it generally cannot be replaced by a metal. A hydrogen atom linked with oxygen (O — H bond) is considerably more "mobile" and is capable, for example, of being replaced by a metal when treated with metallic sodium. If hydrogen is linked to a fluorine atom (or any other halogen), it can be readily replaced by a metal when treated with hydroxides of various metals; the H — F bond can be broken even through the action of water.

The different chemical character of hydrogen in the C — H, O — H and F — H bonds is due to the different polarity and polarizability of these linkages.

The *polarity of a bond* is determined by the electronegativity of the linked atoms, i.e., by the ability of the atoms in a molecule to attract electrons**.

The more electronegative an atom is, the stronger its attraction for electrons.

---

* The valence state of the atoms is very important. It should be pointed out that sometimes there is a strong atomic interaction between atoms which are not directly linked.

** This concept of electronegativity was formulated by Pauling [29]. Nekrasov formulated the concept of electronegativity differently [30]. According to Nekrasov, the electronegativity of an atom is the energy of attraction of an electron cloud of the valence bond by that atom. In other words, it is the energy of attraction by a system, consisting of the nucleus and the complete electron shells surrounding the nucleus, and of a new electron starting the formation of the next quantum layer. Pauling's concept of electronegativity is more widely recognized.

Given below by way of example are the electronegativities of several elements (in electron-volts):

| | | | | | |
|---|---|---|---|---|---|
| H | 2.2 | Si | 1.8 | As | 2.0 |
| C | 2.5 | P | 2.1 | Se | 2.4 |
| N | 3.0 | S | 2.5 | Br | 2.8 |
| O | 3.5 | Cl | 3.0 | I | 2.5 |
| F | 4.0 | | | | |

It should be noted that the terms "electronegativity" and "electronegative element" should be used rather carefully [31], because even the most "electronegative" elements in some compounds exhibit certain electron-donor properties.

For example, oxygen, the most electronegative element of the sixth group of Mendeleyev's table, forms compounds, in which it acts as a donor of two unshared $2s^2$ and $2p^2$ electrons.

Elements of the seventh group have considerable electron affinity and a tendency to form an inert gas shell $s^2p^6$. However, the structure of a large number of compounds is determined by the donor properties of Cl, Br and I, for example, all the complexes with $PdCl_2$ in which chlorine forms two equal bonds (thus, chlorine with an electronegativity of 3.0 is a donor while palladium with an electronegativity of 1.35 is an acceptor of electrons).

One should not take the simplified view of the electronegativity of chlorine exclusively as a tendency for the formation of an anion with an $s^2p^6$ shell. Chlorine may act as acceptor with its vacant $d$-orbitals, if its partner exhibits donor properties (for example, in the molecules of vinyl chloride and chlorobenzene).

Insignificant donor properties, apparently, may be found even in fluorine, for example, in the molecules of sulphur hexafluoride [32] and in acetyl fluoride.

The important atomic characteristics are the energy of electron affinity and ionization potential.

The electron affinity of an atom is determined by the energy released when an electron is added to a neutral atom. For example, some of the values of electron affinity energies (in electron-volts) are: H (0.754), C (1.1), O (1.47), F (3.6), Cl (3.8), Br (3.5), I (3.2).

*Ionization potential* is the field tension at which the removal of an electron from a neutral atom takes place; ionization potential is directly related to ionization energy.

Below are given the ionization potentials of some neutral atoms (in electron-volts):

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| H | 13.6 | Ag | 7.6 | Al | 6.0 | S | 10.3 |
| He | 24.5 | Be | 9.3 | C | 11.2 | F | 17.42 |
| Li | 5.4 | Mg | 7.6 | Si | 8.1 | Cl | 13.0 |
| Na | 5.1 | Ca | 6.1 | N | 19.6 | Br | 11.8 |
| K | 4.3 | Hg | 10.4 | P | 11.0 | I | 10.5 |
| Cu | 7.7 | B | 8.3 | O | 14.3 | | |

Naturally there is a definite correlation between the values of electron affinity of a given atom, its ionization potential and electronegativity.

For instance, the greater the electron affinity of an atom, the greater its ionization potential and electronegativity.

The polarity of different bonds may be quantitatively characterized by the difference in electronegativity of the atoms forming these bonds. The greater this difference the more polar the bond.

The differences of electronegative ($\Delta$) bonds between some atoms are given below:

| *Bond* | $\Delta$ | *Bond* | $\Delta$ |
|---|---|---|---|
| C—H | 0.4 | C—N | 0.5 |
| Si—H | 0.3 | C—O | 1.0 |
| N—H | 0.9 | C—S | 0.5 |
| O—H | 1.4 | C—F | 1.5 |
| H—F | 1.9 | C—Cl | 0.5 |
| H—Cl | 0.9 | C—Br | 0.3 |
| H—Br | 0.7 | C—I | 0.0 |
| H—I | 0.4 | Br—Cl | 0.2 |

From the given $\Delta$ values, in particular, it is apparent that the polarity of bonds of hydrogen with carbon, oxygen and fluorine increases in the order $C - H < O - H < F - H$.

Another important factor which should be taken into account in considering the interaction of directly linked atoms is the polarizability of the atoms and the *polarizability of their bonds* which is determined by it.

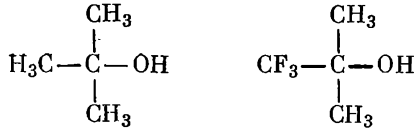
For instance, the ethylene molecule is nonpolar, but it readily adds electrophilic compounds, because the $\pi$ bond is readily polarized under the influence of the attacking reagent:

$$CH_2{=}CH_2 \longrightarrow \overset{\delta+}{CH_2}{=}\overset{\delta-}{CH_2}$$

The high reactivity of alkyl iodides (for example, in reactions of nucleophilic substitution) may be wholly explained by the ease of polarization of the C — I bond, because in the unreacted molecule this bond (unlike C — F, C — Cl, and C — Br bonds) is practically nonpolar ($\Delta = 0$). The polarizability of an atom increases as its electronegativity decreases, because, naturally, the more difficult it is to remove electrons from the atom, the more difficult it is to deform its electronic shell, i.e., to polarize it. On the other hand, polarizability grows with the size of the electronic shell of an atom.

Thus the interaction of atoms directly linked with each other is determined by their nature (electronegativity, in particular) or, in other words, by the polarity and polarizability of the bond between them.

Rather important and extremely interesting is the problem of atomic interaction of atoms which are not directly linked with each other but are separated by a system of single bonds. There is a large number of facts in organic chemistry confirming the interaction of atoms not bonded with each other. An example of such an interaction in alcohols is the difference in properties of trimethyl carbinol and trifluoromethyldimethyl carbinol:



While the acidic properties of trimethyl carbinol are very weak, trifluoromethyldimethyl carbinol is an acid capable of replacing carbonic acid from its salts.

The most characteristic difference is the difference in the strength of acids and bases, for example, in the strength of fatty acids, when one of the hydrogen atoms in the hydrocarbon chain is replaced by F, Cl, Br, I, $NO_2$, CN, $CH_3$, etc.

Thus, the dissociation constants of substituted acetic acids given below show that halides which are not directly bound with the hydrogen atom of the carboxyl group exhibit an influence, different in each particular case.

Experimental data show that this influence weakens as the number of intermediate atoms in the chain increases, as is evident from the following series of ω-chlorosubstituted acids:

| | $K \times 10^5$ |
|---|---|
| $CH_3(CH_2)_nCOOH$ | 1.35-2 |
| $ClCH_2COOH$ | 155 |
| $ClCH_2CH_2COOH$ | 8.5 |
| $ClCH_2CH_2CH_2COOH$ | ~3.0 |
| $ClCH_2CH_2CH_2CH_2COOH$ | ~2.0 |

The dissociation constant of δ-chlorovaleric acid is close in value to that of the unsubstituted acids.

The more electronegative halides influence the dissociation constant of acids to a greater extent.

The dissociation constants of di- and trihalogen acids rival with those of mineral acids.

| | $K \times 10^5$ |
|---|---|
| $HCH_2COOH$ | 1.76 |
| $ICH_2COOH$ | 75 |
| $BrCH_2COOH$ | 138 |
| $ClCH_2COOH$ | 155 |
| $FCH_2COOH$ | 217 |
| $Cl_2CHCOOH$ | 5,140 |
| $Cl_3CCOOH$ | 121,000 |
| $H_3PO_4(K_1)$ | 752 |
| $H_2SO_3(K_1)$ | 1,540 |
| $HIO_3$ | 16,900 |

The influence of a halogen atom upon a carboxyl group not directly linked with it is due to the following.

The C — Cl linkage possesses electrical asymmetry which manifests itself, for instance, in a definite dipole moment, Cl being the negative end of the dipole.

The carbon atom linked with chlorine carries a small positive charge. This makes an electron pair from the neighbouring carbon atom shift in its direction. The latter carbon atom then acquires a certain positive charge, and so forth.

Thus the electric asymmetry of the Cl — C bond is not localized within the confines of the two atoms but is transferred along the entire molecule, as a result of which the hydrogen of the carboxyl group acquires the property of being removed more easily in the form of a proton (for instance, in chloroacetic acid as compared with acetic acid).

Such an effect of atoms not directly linked with each other is called inductive effect and is generally represented graphically as follows:

$$Cl \leftarrow CH_2 \leftarrow \overset{\overset{O}{\parallel}}{C} \leftarrow O \leftarrow H$$

(the arrows indicate the direction of inductive shift of electron pairs).

A characteristic property of the inductive effect is that it weakens quickly, "fades away" along a chain of single bonds.

If an atom or a group of atoms is electronegative, it pulls away the electron pair from the neighbouring atom, causing a gradually diminishing inductive shift of electronic pairs of other bonds in the same direction (as in chloroacetic acid). In such a case the atom or group of atoms are said to exhibit a *negative inductive effect* ($-I$). Conversely, if an atom or a group of atoms repulses an electron pair, then it is said to exhibit a *positive inductive effect* ($+I$).

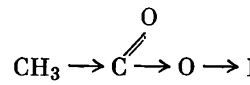
Methyl or any alkyl group may serve as an example of a group of atoms exhibiting a positive inductive effect. This is quite apparent from a comparison of the dissociation constants of formic and acetic acids.

$$H-\overset{\overset{O}{\parallel}}{C}-O-H \quad (K = 17.6 \times 10^{-5})$$

$$CH_3-\overset{\overset{O}{\parallel}}{C}-O-H \quad (K = 1.76 \times 10^{-5})$$

Substitution of the methyl group for the hydrogen combined with carbon in the molecule of formic acid decreases the dissociation constant tenfold. Consequently, the methyl group affects the mobi-

lity of the carboxyl group hydrogen with which it is not directly linked. The hydrogen in the carboxyl of acetic acid is linked more strongly to the oxygen than is the case in formic acid, because of the positive inductive effect of the methyl group:



Data obtained in a study of the strengths of various substituted acids, and other experimental evidence give grounds to arrange substituents in the following order depending on their inductive effects*.

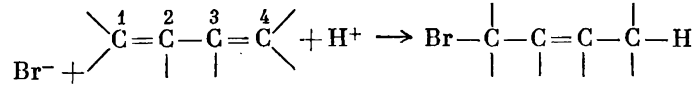
$$\underbrace{F > Cl > Br > I > OCH_3 > C_6H_5}_{-I}$$

$$\underbrace{CH_3 < C_2H_5 < CH(CH_3)_2 < n\text{-}C_3H_7 < C(CH_3)_3}_{+I}$$

The inductive effect of hydrogen is taken as zero. It was chosen as a basis for comparison with other atoms or groups of atoms.

In the molecules of aliphatic compounds containing conjugate bonds and in molecules of aromatic compounds atomic interactions occur predominantly in another way, qualitatively different from the inductive interaction of atoms. To clarify the nature of this interaction let us consider, for example, the properties of systems with conjugated double bonds in aliphatic compounds.

The most characteristic of the chemical properties of systems with two conjugated double bonds is the course of 1,4 additions. In these reactions the attacking molecules or their parts (ions, radicals) add to the terminal (first and fourth) atoms of the conjugated system, a new double bond being formed between the second and the third atom, for example:



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* The fact that in the series $H < CH_3 < C_2H_5 < CH(CH_3)_2 < CH_3CH_2CH_2 < C(CH_3)_3$ the positive induction effect increases (electronegativity decreases), is apparent, for example, from a comparison of the first ionization potentials (of chlorination) of the following compounds:

| | | | |
|---|---|---|---|
| HCl . . . . . | 12.84 eV | $CH_3CH_2CH_2Cl$ . . | 10.7 eV |
| $CH_3Cl$ . . . . . | 11.25 eV | $(CH_3)_3CCl$ . . . . | 10.2 eV |
| $C_2H_5Cl$ . . . . | 10.89 eV | | |

A similar sequence has been found in the increase of dipole moments of alkyl benzenes.

Besides, such systems are generally more reactive (primarily because of the increased reactivity of the first and the fourth atoms) and may enter into reactions not characteristic of molecules with isolated double bonds. Such are reduction of the systems

$$\overset{1}{C}=\overset{2}{C}-\overset{3}{C}=\overset{4}{C} \quad \text{and} \quad \overset{1}{O}=\overset{2}{C}-\overset{3}{C}=\overset{4}{C}$$

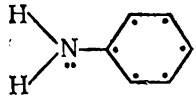
by nascent hydrogen, addition to the former systems of alkali metals and their metalloorganic compounds, addition of the anions $CN^-$, $SO_3H^-$ and $R^-$ (in RMgX) to the fourth (carbon) atom of the latter system, etc.

The chemical properties of conjugated systems show that the double bonds contained in them differ from isolated double bonds. This difference is due to the specific nature of interaction between the unsaturated atoms of conjugated systems, which differs qualitatively from the inductive effect: it may be explained by the interaction of the shared $\pi$ electrons of two or more conjugated double bonds. For this reason it has been suggested that this type of interaction between atoms be called *conjugation of bonds.*

Molecules with conjugated double bonds have certain specific physical properties, for example, a higher energy of formation than the isomeric molecules with isolated double bonds, a certain equalization of interatomic distances and high polarizability of their electronic system of bonds.

These physical constants characterize the structure of the nonreacting molecule. Consequently, they indicate that conjugation of double bonds exists also in the nonreacting molecule. It has been suggested to call the result of conjugation of bonds in the nonreacting molecule *static effect of conjugation.*

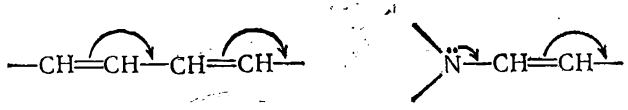
As has been indicated, the nature of conjugation of double bonds may be interpreted as a result of the high mobility of $\pi$ electrons, which shift in the conjugated system as a whole. The part of a $\pi$ electron pair of one of the linkages of the conjugated system may be played by an unshared pair of *p* electrons of such atoms as N, O, S, etc., for instance, in the aniline molecule:



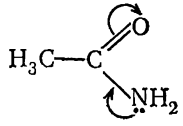
Here the unshared *p*-electron pair of nitrogen reacts with the $\pi$ electrons of the benzene ring, resulting in lower basicity of the amine group of aniline (relative to that of a fatty amine) and higher nucleophilic reactivity of the *ortho-* and *para*-carbon atoms of the aromatic ring compared to that of the carbon atoms of the benzene molecule.

This example shows clearly that the term "conjugation of bonds" indicates essentially a definite type of interaction between the electronic systems of atoms, and that valence electrons take part in this interaction.

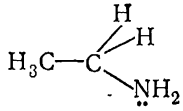
In order to represent this type of interaction by structural formulas, the shifts of the $\pi$ electrons are indicated by bent arrows drawn from the C = C double bond to the single C — C bond or from the atom with an unshared pair of electrons to a single bond in the direction of shift:



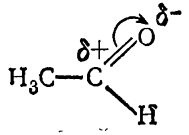
In the molecule of acetamide, for example, the unshared pair of electrons is conjugated with the $\pi$ bond, and this is generally written as follows:



The distribution of electron density in the acetamide molecule is determined by the competition between the O and N atoms in accordance with their electron affinity; the shift of the unshared pair of electrons of nitrogen toward the carbon accounts for the lowering of the basic properties of the amino group of acetamide compared with the amino group in the amine:



and at the same time, for the lowering of the electrophilic reactivity of the carbonyl group (more precisely, of the carbon atom of this group) relative to the carbonyl group in aldehydes:



From the above it follows that to elucidate the nature of static conjugation (and to elucidate the nature of atomic interactions in general) the properties of substances resembling each other more or less in chemical structure must be compared.

When substances containing conjugated double bonds take part in reactions, they exhibit a dynamic effect of conjugation alongside

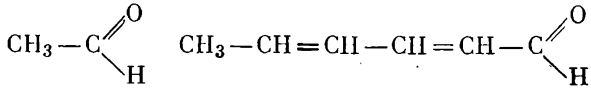
the static effect, the former effect usually being the more important one. It consists in redistribution of the electron density in a system with conjugated bonds (polarizability) at the instant of the chemical reaction under the influence of the attacking reagent. As the dynamic influences in molecules with conjugated bonds apparently lead, in the great majority of cases, to the same consequences for the reactivity of a substance as the static ones, and because they are usually difficult to distinguish from the latter, they are also designated by bent arrows. The reaction of hydrogen halides with butadiene (which is not polar) may serve as an example of a reaction in which a dynamic conjugation is exhibited:

$$\overset{+}{H} + CH_2=CH-CH=CH_2 + X^- \longrightarrow \underset{H}{CH_2}-CH=CH-\underset{X}{CH_2}$$

It is a remarkable feature of the mutual influence of atoms in systems with conjugated double bonds that this influence is transmitted without weakening substantially along the chain of conjugated bonds

$$(-CH=CH-CH=CH-\ldots)$$

This transfer of mutual influence is so complete that in a number of cases there is no difference at all between the mutual influence of atoms linked directly to one another and of atoms separated by a system of conjugated bonds, as is evident from a comparison of the chemical properties of such compounds. For example, the difference between acetaldehyde and sorbic aldehyde:



is that in the former the methyl group is linked directly to the carbonyl group, while in the latter it is separated from the carbonyl group by a chain of four carbon atoms. In spite of this, the methyl group of sorbic aldehyde is affected by the far removed carbonyl group just as much as in acetaldehyde. Thus, its hydrogen atoms are "mobile" and sorbic aldehyde (like acetaldehyde) is capable of condensation:

$$R-CHO + CH_3CHO \longrightarrow R-CH=CH-CHO + H_2O;$$

$$R-CHO + CH_3-CH=CH-CH=CH-CHO \longrightarrow$$

$$\longrightarrow R-CH=CH-CH=CH-CH=CH-CHO + H_2O$$

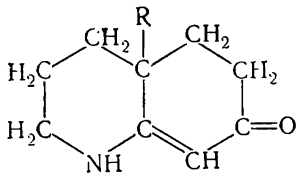
Esters of sorbic acid $CH_3-CH=CH-CH=CH-COOR$ are capable of condensation through their ε-hydrogen atoms in the same way as ethyl acetate through its α-hydrogen atoms. This

remarkable widely known phenomenon in organic chemistry, generally called *vinylogy*, consists in that the system

$$-CH=CH-CH=CH-\ldots$$

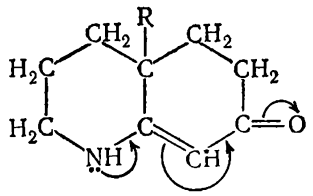
behaves not as a conglomeration of double bonds but as a uniform system effectively transmitting the interaction of atoms.

A characteristic example of conjugation of double bonds is represented by the compound:



Judging from the structural formula, this compound should have the properties of a secondary amine and a ketone. Actually, in chemical properties this compound is an amide (it is devoid of basic properties and does not give the usual carbonyl group reactions).

The amide properties of this compound are due to a conjugation in which the free electron pair of the nitrogen participates:

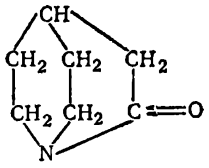


The interaction between the nitrogen and the carbonyl group is here analogous to the interaction in acetamide (page 55)—hence the amide properties of the compound.

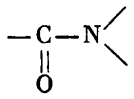
A necessary condition of conjugation is that the axes of the $\pi$ electron (and $p$ electron) clouds be parallel because only then can the electron clouds overlap to form a uniform electronic system which can readily transmit atomic interactions.

If the parallelism of the electron cloud axes is disturbed, the conjugation is weakened. Conjugation is impossible if the electronic cloud axes are perpendicular to each other.

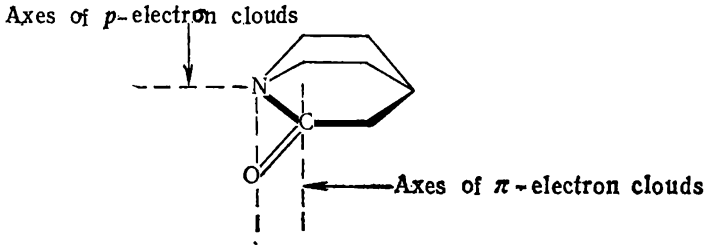
Quinuclidone-2 [33] is a very interesting illustration of this:



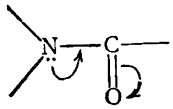
Formally, one would expect quinuclidone-2 to have amide properties because of the amide group present in its molecule.



However, in this rigid bicyclic system the configuration of the nitrogen atom is so fixed that the axes of the free $p$ electron clouds of the nitrogen atom are perpendicular to the axes of the $\pi$ electron clouds of the carbonyl group.

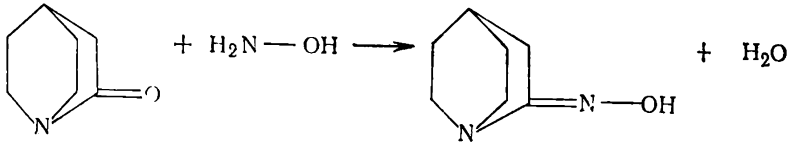



Therefore, conjugation of the type



generally characteristic of the amide group is in this case impossible.

Hence the aminoketone properties of quinuclidone-2. Quinuclidone-2 is basic and participates in reactions characteristic of the carbonyl group of ketones, for instance:




Although the benzene ring (see Chapter 8) does not contain alternate double and single bonds (all its bonds being equivalent), however, in its capacity to transmit the interaction of atoms, it behaves like a system of conjugated bonds.

This can be illustrated by the following simple example: the substitution of a nitro group for one of the hydrogen atoms of water

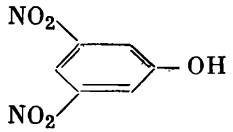
$$H—O—H \longrightarrow O_2N—O—H$$

as is known, results in a sharp increase of the ability of the remaining hydrogen atom to be eliminated as a proton. The nitro group exhibits quite a similar, though weakened, influence when it is separated from the hydroxyl by a benzene ring, for example, in *p*-nitrophenol which is a 565 times stronger acid than phenol.

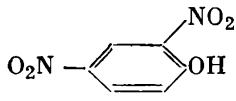
The behaviour of the benzene ring as a system of conjugated double bonds explains the phenomenon that the interaction of atoms or groups of atoms introduced into the benzene ring is manifested much more strongly when they are in the *ortho-* or *para*-position relative to each other than in the *meta*-position.

Thus, comparison of the dissociation constants of isomeric nitrophenols shows that $K = 0.75 \times 10^{-7}$ for the *ortho*-isomer, and $K = 0.96 \times 10^{-7}$ for the *para*-isomer, whereas for the *meta*-isomer $K = 1.0 \times 10^{-8}$ (at 25°).

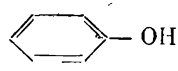
A still more vivid example is that of 3,5- and 2,4-dinitrophenols:




$K = 2 \times 10^{-7}$




$K = 1 \times 10^{-4}$




$K = 1.7 \times 10^{-10}$

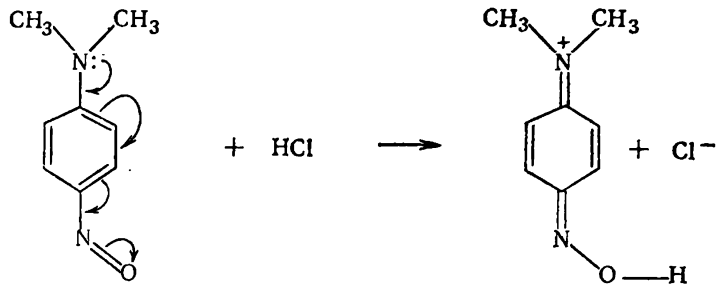
If these data are compared with the dissociation constant of phenol, $K = 1.7 \times 10^{-10}$, it becomes clear that the presence of the nitro group in the *ortho-* or *para*-position has a greater influence on the dissociation constant of phenol than in the *meta*-position. Thus the influence of a nitro group drawing away electrons is transmitted more effectively from the *ortho-* and *para*-positions of the benzene ring than from the *meta*-position. If in this case the phenomenon were due only to inductive effect, the influence of the nitro group would weaken in the order *ortho* > *meta* > *para*.

Many other examples are known where the interaction of atoms in the benzene ring shows up sharply if they are in the *ortho-* or *para*-position to each other, and much weaker if they are in the *meta*-position. Thus, the reactivity of chlorine in *ortho-* and *para*-nitrochlorobenzenes is much higher (with reference to nucleophilic reagents) than in *meta*-nitrobenzene; salts of *ortho-* and *para*-nitroaniline are unstable, in contrast to those of *meta*-nitroaniline; *ortho-* and *para*-nitrophenols exhibit tautomerism (while the *meta*-isomers do not), and so on.

Some peculiarities of atomic interactions transmitted through the benzene ring may be studied in a number of more complex cases.

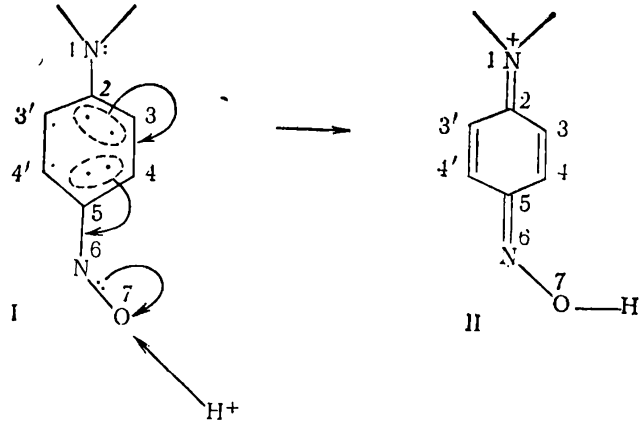
For instance, a good example of the interaction of nitrogen and oxygen atoms, materialized by conjugation through the benzene

ring, is the reaction of *p*-nitrosodimethylaniline with an acid:




In this case the reaction centre is transferred* from the nitrogen atom of the dimethylamino group which possesses basic properties, to the oxygen atom, whose basic properties are generally weak. It is apparent from this example that it makes absolutely no difference whether the benzene ring is depicted as a system of alternating double and single bonds, or in the form of a hexagon with six $\pi$ electrons (one for each carbon atom).

Let us consider system II resulting from the addition of a proton to *p*-nitrosodimethylaniline (I).




The proton adds to the oxygen atom-7 through the agency of the two electrons of the N = O group. In such a case the electron pair necessary for the formation of the double bond C = N (5,6) is obtained from the benzene ring ($\pi$ electrons 5 and 4 or $\pi$ electrons 5 and 4'), resulting in a quinoid structure. The double bond 3,4 in system II could form only through $\pi$ electrons 2 and 3, and the double bond N = C (1,2) only through the free electron pair of the amine nitrogen atom.

* This idea was suggested by Nesmeyanov.

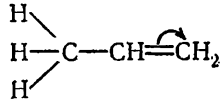
Thus, although the benzene molecule contains a system of equally distributed π electrons, at the instant of reaction electronic shifts take place in the benzene ring which correspond to the rules of conjugation of double bonds*.

We have discussed the widespread and long known phenomenon in organic chemistry, that of conjugation of double bonds (π,π conjugation).

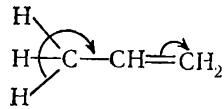
The concepts of conjugation of a single bond with a double one (σ,π conjugation) and of two single bonds (σ,σ conjugation) were developed recently by Nesmeyanov, who pointed out a number of analogies of chemical behaviour of π,π-, σ,π-, and σ,σ-conjugated systems, for example, in 1,4-addition reactions [44].

Certain experimental data on the conjugation of single and double bonds have been available for a long time.

From the standpoint of current electronic concepts the order of addition of the elements of hydrogen halides, according to Markovnikov's rule, to propylene, for example, is due to electrical asymmetry of its double bond, owing to the influence of the methyl group:



This asymmetry is evident, for example, from the dipole moment of the propylene molecule (0.35 D). The shift of the π electron pair is apparently due to a slight shift of the σ electrons of the methyl group C — H bonds in the same direction. Usually it is expressed as follows:

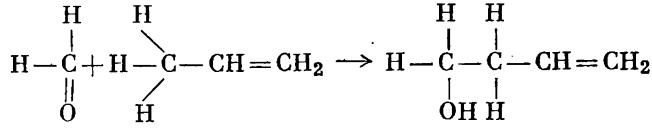


This comprises the static effect of conjugation of single and double bonds (σ,π conjugation).

Evidently, such a distribution of the electron cloud in the molecule must not only change the chemical nature of the double bond to some extent, but also that of the C — H bonds of the methyl group. One could expect that the hydrogen atoms of the methyl group of propylene should be more reactive than those of propane. Experimental data confirm this supposition; for instance, the hydrogen atoms of the propylene methyl group can easily be eliminated as protons in liquid deuteroammonia ($ND_3$) and replaced by deuterium.

* In this discussion we naturally disregard the fact that the benzene ring in the nitrosodimethylaniline molecule, unlike the benzene molecule, no longer possesses a fully symmetrical cloud of π electrons.

Propylene is capable of reacting with formaldehyde in an aldol-type condensation*:

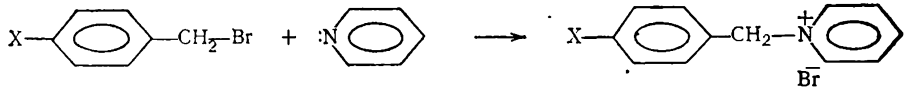


like in the case of aldehydes containing α-hydrogen atoms.

Other reactions are known illustrating the higher reactivity of hydrogen atoms linked with an α-carbon atom (in relation to the double bond) compared with the hydrogen atoms of saturated hydrocarbons.

Now, one may ask whether σ,π conjugation with the participation of C — H linkages is of the same origin as the positive inductive effect of alkyl groups, in other words, whether these effects are identical. The answer is negative, primarily because the sequence of values of the inductive effects of alkyl groups, derived from a study of compounds with single bonds, is not observed when we pass over to conjugate (σ,π), unsaturated and aromatic compounds.

In 1935 Baker and Nathan [34] studied the influence of alkyl substituents in the molecules of *para*-alkylbenzylbromides on the rate of reaction of these substances with pyridine:



In all the cases the reaction proceeded faster than with the unsubstituted benzyl bromide, but the sequence of influence was the reverse of what should have been expected with reference to the inductive effects of alkyl groups. The reactions went the fastest with the methyl substituted compound, and the slowest with the *tert*-butyl derivative:

$$CH_3 > (CH_3)_2CH > (CH_3)_3C$$

On the basis of these facts the conclusion was drawn that, besides the inductive effect, alkyl groups are capable of exhibiting another (weak ) effect due to the ability of the σ electrons of C — H linkages to react with the π electrons of the neighbouring bond. This phenomenon was called *hyperconjugation* by Baker and Nathan.

Later the study of hyperconjugation [35, 36] was devoted mainly to investigation of the interaction of methyl or methylene groups with double bonds, that is, to conjugation of H — C with C = C

* This reaction takes place in the presence of boron fluoride or copper, silver and beryllium halides as catalysts.

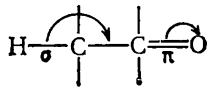
(or C — O) linkages, as a result of which the terms "Nathan-Baker effect" or "hyperconjugation" were applied to the C — H bond.

Hyperconjugation is a very important but particular case of σ,π-conjugation.

It should be pointed out that there is no convincing evidence so far concerning the effect of hyperconjugation on the physical properties of substances (heats of formation, bond lengths).

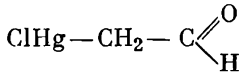
At the same time the existence of "dynamic hyperconjugation" which shows up in the reactivity of substances is unquestionable, though its nature needs further study [35-41].

In the case of the system:

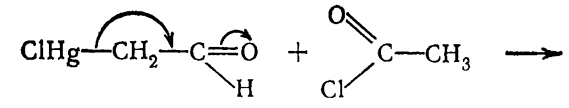


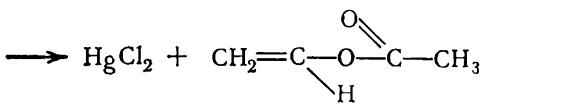
the conjugation of σ and π bonds is more pronounced because of the higher electronegativity of the oxygen atom compared with the carbon atom. Thus the considerable reactivity of the α-hydrogen atoms of aldehydes, ketones and esters is well known. If in such a system the hydrogen atom is replaced by a more polarizable atom, say, mercury, the σ,π conjugation will be more pronounced.

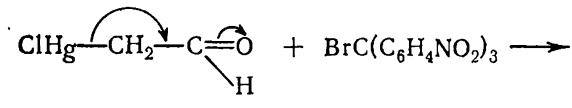
This can be illustrated, for instance, by chloromercuricacetaldehyde:

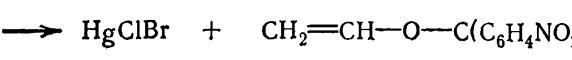


The conjugation of the Hg — C and C = O bonds is of such an extent, that a number of reactions of this substance involving elimination of mercury fail to take place at the point where the Hg — C bond is broken, but occur at the oxygen atom of the C = O group instead, that is, these reactions involve a transfer of the reaction centre, for example [42]:

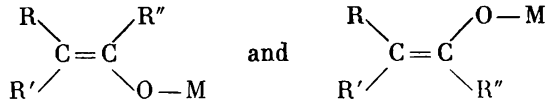




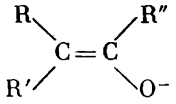




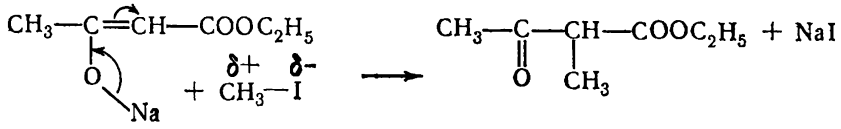
Conjugation of single with double bonds accounts for a number of important phenomena in the reactivity of molecules containing the system M — O — C = C, i.e., the metal enolate (or phenolate) system. Using lithium, sodium and magnesium enolates of β,β-diphenylpropiomesitylene as examples, Nesmeyanov and Sazonova [43] have proved that the M — O bond is covalent and not ionic, because the enolates mentioned exist in two stereoisomeric forms (*cis* and *trans*):



Consequently all the earlier hypotheses attributing the dual reactivity (at O and at C) of such compounds to different properties of the anion



are in general incorrect.* Actually dual reactivity is due to conjugation of M — O and C = C bonds, as, for example, in the exceptionally important case of sodium acetoacetic ester:



Conjugation of two single bonds, separated by one double or by one single bond, was studied by Nesmeyanov and his students mainly on the products of addition of heavy metal salts ($HgCl_2$, $SbCl_3$, $AsCl_3$, etc.) to ethylene and acetylene:

$$M—CH_2—CH_2—X \text{ and } M—CH=CH—X$$

In these systems conjugation of M — C and C — X bonds is clearly indicated. Thus, for example, in the compound ClHg — CH = = CH — Cl, ClHg is readily eliminated as a cation and Cl as an anion under the influence of a large number of reagents; acetylene is formed simultaneously, for example:

$$ClHg—CH=CH—Cl+KI \longrightarrow KCl+HgClI+H—C\equiv C—H$$

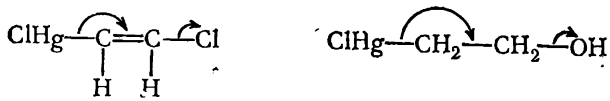
* A large number of cases are known, however, where metal enolates react under conditions whereupon they should have been ionized (e.g., in water-alcohol mixtures); in these cases the reason for dual reactivity should be sought in the properties of the enolate anion.

In the reaction

$$HO-CH_2CH_2-HgCl+HCl \longrightarrow H_2O+CH_2=CH_2+HgCl_2$$

he chloromercury group is readily eliminated as a cation, and he hydroxyl as an anion.

This type of readily occurring reaction is due to the conjugation of the Hg — C and C — Cl bonds in the first case and of the Hg — C and C — OH bonds in the second:



Thus, in their main manifestations σ,π conjugation and σ,σ conjugation are like π,π conjugations, though they are not so pronounced.

This similarity becomes especially clear-cut if we compare typical reactions of π,π-conjugated systems with those of σ,π- and σ,σ-conjugated systems.

$$\left.\begin{array}{l} \overset{1}{C}H_2=\overset{2}{C}H-\overset{3}{C}H=\overset{4}{C}H_2+HCl \longrightarrow \\ \qquad \longrightarrow H-\overset{1}{C}H_2-\overset{2}{C}H=\overset{3}{C}H-\overset{4}{C}H_2-Cl \\ \overset{1}{C}R_2=\overset{2}{C}R-\overset{3}{C}R=\overset{4}{O}+R'MgX \longrightarrow \\ \qquad \longrightarrow R'-\overset{1}{C}R_2-\overset{2}{C}R=\overset{3}{C}R-\overset{4}{O}MgX \end{array}\right\} \pi,\ \pi \text{ conjugation}$$

$$\left.\begin{array}{l} \overset{1}{Cl}Hg-\overset{2}{C}H_2-\overset{3}{C}H=O+CH_3COCl \longrightarrow \\ \qquad \longrightarrow \overset{1}{H}gCl_2+\overset{2}{C}H_2=\overset{3}{C}H-\overset{4}{O}-COCH_3 \\ \overset{1}{Na}-\overset{2}{O}-\overset{3}{C}(CH_2)=\overset{4}{C}\begin{cases}H\\COOC_2H_5\end{cases}+CH_3I \longrightarrow \\ \qquad \longrightarrow \overset{1}{Na}I+\overset{2}{O}=\overset{3}{C}(CH_3)-\overset{4}{C}H\begin{cases}CH_3\\COOC_2H_5\end{cases} \end{array}\right\} \sigma,\ \pi \text{ conjugation}$$

$$\left.\begin{array}{l} Cl\overset{1}{H}g-\overset{2}{C}H=\overset{3}{C}H-\overset{4}{C}l+RMgBr \longrightarrow \\ \qquad \longrightarrow R\overset{1}{H}gCl+\overset{2}{C}H\equiv\overset{3}{C}H+\overset{4}{C}lMgBr \\ Cl\overset{1}{H}g-\overset{2}{C}H_2-\overset{3}{C}H_2-\overset{4}{O}H+HCl \longrightarrow \\ \qquad \longrightarrow \overset{1}{H}gCl_2+\overset{2}{C}H_2=\overset{3}{C}H_2+H_2\overset{4}{O} \end{array}\right\} \sigma,\ \sigma \text{ conjugation}$$

It must be pointed out that *conjugation of bonds* is to be undertood as a manifestation of a definite type of *atomic interaction.*

The ideas concerning conjugation of bonds are a further development of the problem of atomic interactions in molecules. These concepts have made it possible now to understand and unify a large number of phenomena in organic chemistry which seemed very puzzling before.

The concept of conjugation of bonds lays open the nature of atomic interactions and enables systematization of available experimental data. It would be wrong to separate the question of the conjugation of bonds from the problem of atomic interactions. The chemical bond is only a form of interaction of atoms, and, naturally, cannot be considered independently of the atoms.

### Quantum-Mechanical Methods of Calculating Molecules of Organic Compounds

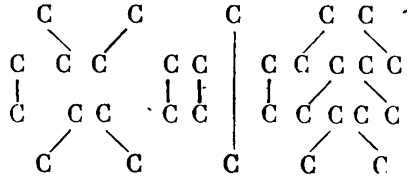
The progress of theoretical chemistry and the development of quantum mechanics made possible approximate quantitative calculations of molecules. Two most important methods of calculation are known: the method of electron pairs, known also as the valence bond method, and the method of molecular orbitals. The former method, worked out by Heitler and London for the hydrogen molecule, was widely used in the thirties of this century. Currently the method of molecular orbitals (Hund, Hückel, Mulliken, Herzberg, Lenard-Jones) is acquiring greater importance.

**Method of Electron Pairs (Valence Bond Method).** In this approximate method of calculation the state of the molecule is described by a so-called wave function $\psi$, which is composed according to a definite rule of a series of terms:

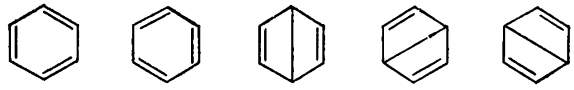
$$\psi = C_1\psi_1 + C_2\psi_2 + C_3\psi_3 + \ldots + C_n\psi_n$$

The sum of these terms must take into consideration all the possible combinations which may arise as a result of bonding of the carbon atoms in pairs through $\pi$ electrons.

To facilitate calculation of the wave function $\psi$, the individual terms ($\psi_1$, $\psi_2$, etc.) are conventionally represented graphically as corresponding valence schemes, which are used as auxiliary means in the mathematical calculation. For example, when a molecule of benzene is calculated by this method, taking into consideration only $\pi$ electrons, the number of such terms is five. The following valence schemes correspond to these terms:



These valence schemes are often shown together with the σ bonds, for example, for benzene:



I II III IV V

Such valence schemes are called "unperturbed structures" or "limiting structures"*.

The numerical coefficients (weights) of the functions $\psi_1$, $\psi_2$, $\psi_3$, etc., of the different limiting structures in the wave function are the greater, the smaller the energy calculated for the corresponding structure. The electronic state corresponding to the wave function $\psi$ is more stable than any of the electronic states, designated by the functions $\psi_1$, $\psi_2$, $\psi_3$, etc.; and the energy of state designated by the function $\psi$ (of the real molecule) is naturally smaller than any of the energies of the limiting structures.

In calculating a benzene molecule by the method of electron pairs five limiting structures (I-V) are taken into account. Two of them are identical with the classical Kekulé formula and three with the Dewar formula. Since the energy of the electronic states, corresponding to the limiting structures III-V, is higher than for structures I and II, the contribution of structures III, IV and V to the total wave function of the benzene molecule is smaller than that of structures I and II. For the first approximation the two equivalent Kekulé structures are sufficient to represent the electron density distribution in the benzene molecule.

### Theory of Resonance

About 30 years ago Pauling developed qualitative empirical concepts, analogous in some respects to the method of electron

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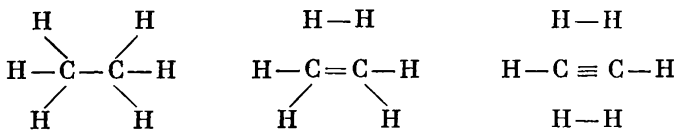
* If the ethane molecule is calculated to the same approximation, then among others, distributions of electronic spins among the atoms with the following valence schemes should be taken into account:



Unlike the case of benzene these schemes, with the exception of the left-hand one, no longer resemble the structural formula of ethane. From the above it is clear that in general the valence schemes have an entirely different content than conventional structural formulas.

pairs; he called these concepts "theory of resonance"*. According to the basic premise of this theory, any molecule, for which several classical structural formulas can be written, cannot be correctly represented by any of those formulas (limited structures) taken alone, but only by the entire set, by their superposition.

The distribution pattern of the electron density in the molecule is described qualitatively by superposition of the limiting structures (each being taken with a definite weight).

The limiting structures do not correspond to any real electronic states in unexcited molecules, but it is not impossible that they may materialize in an excited state or at the moment of a reaction.

The above described qualitative aspect of the theory of resonance** coincides with the concept of mesomerism, developed somewhat earlier by Ingold [58] and independently by Arndt.

According to this concept the true state of the molecule is intermediate ("mesomeric") among the states represented by two or more of the "limiting structures", which may be written for the given molecule, applying the rules of valence.

Besides this basic premise, the theory of mesomerism includes well developed concepts of electron shifts, the grounding, interpretation and experimental proof of which are due to a considerable extent to Ingold [59].

According to Ingold the mechanisms of electronic shifts (electronic effects) differ depending on whether the atomic interaction takes place through a chain of simple or conjugated double bonds. The first case is one of inductive effect $I$ or $I_s$, the second, of mesomeric effect $M$ (static effect of conjugation). In a reacting molecule the polarizability of the electron cloud may be achieved by the induction mechanism. Such an electronic shift is called inducto-

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* Sometimes the method of electron pairs is included in the concept of the theory of resonance, it is then called the resonance method. The theory of resonance in its original form is best presented in Pauling's book *The Nature of the Chemical Bond* [29].

Wheland formulated four conditions of resonance [45]: (1) Resonance can take place only among structures corresponding to equivalent or approximately equivalent relative positions of all the atomic nuclei. (2) Resonance cannot take place among structures differing sharply in arrangement of their electrons. (3) Resonance cannot take place among structures with different numbers of unpaired electrons. (4) If the former conditions are met, resonance may take place, but it is significant only when the different structures have the same or approximately the same stability (that is, energy).

** In the literature the qualitative theory of resonance developed by Pauling is often equated with one of the approximate methods of quantum mechanics—the method of electronic pairs. The possibilities of this method so far are limited to calculations of relatively simple molecules. Specialists in the field of quantum chemistry (Coulson and others) consider that for complex organic systems another approximate method, the molecular orbital method, has better prospects.

meric effect $I_d$. In molecules with conjugated double bonds (and in aromatic molecules) the polarizability of the electron cloud at the moment of the reaction is due to the electromeric effect $E$ (dynamic effect of conjugation).

As far as methods of portraying molecules are concerned, the resonance concept arouses no fundamental objections. However, this concept lays greater claims. Analogously as the wave function is described by a linear combination of other wave functions $\psi = C_1\psi_1 + C_2\psi_2 + C_3\psi_3$, etc., in the method of electron pairs, the theory of resonance suggests that the true wave function $\psi$ of the molecule can be described as a linear combination of wave functions of the limiting structures.

But from a chemical point of view this analogy is pointless, because mathematics provides no criteria for selecting "resonance structures"; in the method of electron pairs the wave function may be represented not only as a linear combination of wave functions $\psi_1$, $\psi_2$, $\psi_3$, etc., but also as a linear combination of any other functions provided with definite coefficients*. But the selection of limiting structures can be made only on the basis of chemical considerations and analogies.

Thus, in this respect, the resonance concept essentially offers nothing new compared with the concept of mesomerism.

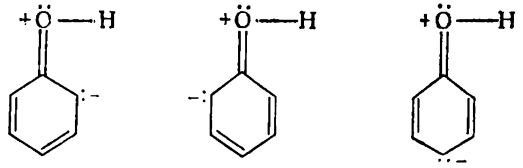
The partisans of the theory of resonance often cite the following crude but vivid analogy of this concept. To describe a mule to a man who never saw one but who knows a horse and a donkey, a mule is said to be a superposition of the two, in which the horse is represented with its weight (coefficient $C_1$), and the donkey with its weight (coefficient $C_2$). Continuing this crude illustration, it can be maintained, that the concept of resonance cannot predict that the mule is a hybrid, to wit, of a horse and a donkey. This has to be arrived at in an independent way. Otherwise, one could select a giraffe as one of the parents and choose the second parent in such a way that mathematically everything would be in agreement.

In representing the distribution of electron density in molecules with the aid of limiting structures it must always be kept in mind that limiting structures taken separately do not correspond to any real physical state and that no phenomenon of "electronic resonance" exists. Many cases are known in the literature where the followers of the resonance concept essentially ascribed to resonance the sense of a physical phenomenon and declared certain limiting structures responsible for definite properties of substances.

Two examples might be mentioned. Pauling explains [30] the acid properties of phenol as follows: "The acidity constant of phenol

* Wheland [45] himself correctly notes: "Moreover, if in equation (1) ($\psi = K_1\varphi_1 + K_2\varphi_2 + \ldots K_n\varphi_n$) another set of $\varphi$ is used, then the molecule whose wave function approaches the function $\psi$ will be described differently, as resonating among an entirely different series of structures.

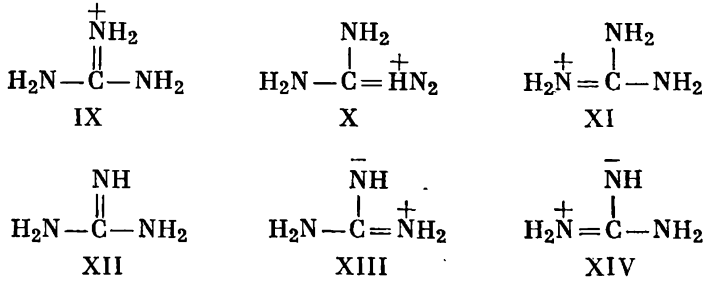
$1.7 \times 10^{-10}$ is much greater than that of aliphatic alcohols. We ascribe this to resonance with the structures F, G, H:



F G H

in which the oxygen atom has a formal positive charge."

Wheland gives the following explanation of the basicity of guanidine: "In certain substances resonance increases the basicity. For example, guanidine is a strong base with $pK = 13.5$, apparently because resonance in the ion among the three equivalent structures IX, X and XI plays a much more significant part than resonance among the corresponding non-equivalent structures XII, XIII and XIV in the neutral molecule":



IX X XI

XII XIII XIV

The possibility for such interpretations to appear is built into many points of the resonance concept. Thus, speaking of "different contributions of limiting structures" to the real state of the molecule easily gives rise to the concept of the actual existence of these correlations. In the resonance concept a real molecule is considered a "resonance hybrid"; this term may give the idea of a supposedly real interaction of limiting structures like hybridization of atomic orbitals.

Finally it should be noted that what is known as "stabilization through resonance" is not due to non-existing resonance, but represents a physical phenomenon, characteristic of conjugated systems. It would be better, therefore, to call this phenomenon stabilization due to conjugation.

The energy of conjugation (energy of delocalization or energy of mesomerism) can be determined experimentally, irrespective of the "energy of resonance", derived from quantum-mechanical calculations. The energy of conjugation is the difference between the

energies of a hypothetical molecule having a formula corresponding to one of the limiting structures and the real molecule.

With the above reservations the method of describing the distribution of electron density in molecules with the aid of several limiting structures can undoubtedly be used alongside other more widespread methods.

The theory of resonance has been criticized by a number of scientists [46, 47, 48].

In 1956 Pauling published a paper "Nature of the Theory of Resonance" [49], which was written in reply to criticism of the theory of resonance by Soviet scientists and by Hückel.

First of all Pauling states correctly that although the theory of resonance has existed for 25 years, there are different opinions as to what it represents.

Then Pauling strives to make the following two points:

1. The criticism of the theory of resonance by Soviet scientists and by Hückel, the basic point of which, in Pauling's opinion, consists in denying the legitimacy of operating with separate actually non-existing resonance structures, is not valid because such "theoretical constructions, idealizations" as bonds C = C, C — C, C — H, etc., have been utilized successfully in organic chemistry for a long time. These bonds, in Pauling's opinion, are in themselves unreal, because it is impossible, for instance, to isolate a single carbon-carbon bond and subject it to experimental investigation.

2. The theory of resonance is not a branch of quantum mechanics; it is predominantly a qualitative theory, a part of the structural theory.

We cannot agree with either of these points.

It is incorrect to draw an analogy between resonance structures and chemical bonds (C = C, C — C, C — H, etc.) as between equal "theoretical constructions" and "idealizations". In chemistry, in general, and in the theory of chemical structure, in particular, the methodological starting point consists in that actually existing atoms are linked in a definite sequence in actually existing molecules. Therefore, chemical bonds of atoms in molecules (understood by us as a definite form of interaction of atoms in molecules) are also real and exist objectively *.

Of course, outside a concrete molecule, the bonds C = C, C — C, C — H are abstractions.

However, these abstractions are quite different from resonance structures. It is a question of the degree of abstraction. The concepts of C = C, C — C, C — H, etc., bonds have a corresponding definite objective reality (definite relations of atoms in real molecules). Nothing corresponds objectively to the concepts of separate resonance structures. These are purely subjective constructions.

It is clear that the analogy between resonance structures and the structural elements of organic chemistry does not apply.

It has already been mentioned above that Pauling in his paper develops an idea, according to which the theory of resonance cannot be considered a branch of quantum mechanics, that it is a qualitative theory, a part of the structural theory.

Pauling writes [49]: "Classical structural theory was developed on the basis of chemical factors alone without any help from physics. The theory of resonance also was in the process of formation before the discovery of quantum mechanics" and further.... "Theory of resonance is a part of this chemical

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* The objective existence of chemical bonds can be maintained on the same basis as the objective existence of universal gravity, electrostatic attraction and repulsion, as well as other forms of interaction of matter.

structural theory which has in the essence an empirical (inductive) basis; it is not simply a part of quantum mechanics."

It is obvious, that Pauling's point of view on this question has undergone evolution. At an earlier date he stated that the basis of the theory of resonance was to be found in quantum mechanics.

He wrote [29]: "There is one basic principle in quantum mechanics which is of essential importance to the majority of questions related to the basic states of molecules. This principle forms the basis of the resonance concept".

Other followers of the theory of resonance also stressed that the theory of resonance leans on quantum mechanics. Thus, Wheland writes [45]: "... the origins of this theory (theory of resonance—O.R.) should be sought out in the depths of quantum mechanics, and, therefore, a strict and complete presentation of the theory can be made only in the language of mathematics."

Finally, without going any further into the question of the relationship of the theory of resonance to quantum mechanics it should be pointed out, that the theory of resonance can hardly be considered a part of the "classical structural theory", that is, the theory of chemical structure. They differ essentially in spirit from each other. The theory of chemical structure has to do only with objectively existing particles (molecule, atom) and with the nature of their reactions (chemical bonds, interactions, etc.). It reflects very important objective laws.

The theory of resonance is characterized by elements of subjectivism.

This subjectivism is evident, for example, from the crude but graphic metaphors given above by Wheland to explain the theory of resonance.

Let us consider another analogy [50]: A traveller in the Middle Ages came across a rhinoceros for the first time and described it as something middling between a dragon and unicorn. This analogy seems to Wheland most fitting: the benzene molecule and rhinoceros have a real existence, but they are described with the aid of Kekulé's (and Dewar's) * structures, the actually non-existing dragon and unicorn.

However, the shortcoming of such a method of description is not that an actually existing object is described with the aid of abstractions. The trouble here is that a traveller in the Middle Ages (depending on his nationality, culture, etc.) could describe a rhinoceros by dozens of other, widely different comparisons, besides that cited by Wheland.

As we have pointed out already, such an approach to the description of molecules inevitably results in the introduction of subjectivism into science.

The basic difference between the theory of resonance and the theory of chemical structure may be formulated briefly as follows: the theory of chemical structure is a theory of molecules while the theory of resonance is essentially a system of ideas of how to represent electron density distributions in molecules according to definite rules.

Thus, the term "theory of resonance" at present actually means a definite way of writing electronic structural formulas.

### Method of Molecular Orbitals (MO Method)

In recent years an approximate quantum-mechanical method of calculation known as the molecular orbital method is receiving a wider and wider application [51, 52]. In using this method there

* The synthesis of Dewar's benzene was recently reported by van Tammelen at the Organic Chemistry Symposium, Columbus, Ohio, June, 1963.—*Tr.*

is no need to resort to any valence schemes of the type of "resonance structures".

The MO method differs from the valence bond method or the method of electron pairs, developed by Heitler and London, in that instead of wave functions, describing electron pairs, it uses the wave functions of a single electron in the field of all the nuclei and other electrons. The electrons of the molecule are distributed over monoelectronic levels with allowance for Pauli's principle, that one molecular orbital can contain only two electrons with opposite spins.

The molecular orbital differs in appearance from the corresponding atomic orbital in that its function is polycentric rather than unicentric; in the simplest case it is bicentric. To find the $\psi$ function it is assumed that a given electron near atom $a$ has a wave function similar to the eigenfunction of atom $\psi_a$; near atom $b$—a wave function similar to $\psi_b$ [the method of linear combination of atomic orbitals is used (LCAO)]:

$$\psi = \sum_i C_i \psi_i$$

where $\psi_i$ is the atomic orbital of the electron at the $i$ atom; summation is carried out over all $i$ atoms, and the coefficients $C_i$ are determined by the variational method so that the energy is a minimum. The following wave equation results for the $H_2^+$ ion

$$\psi = \psi_{(a:1s)} + C\psi_{(b:1s)}$$

where $1s$ stands for the electronic state (the normal, or ground, state) responsible for the formation of the bond. The energy for the state, at which the bond is formed, is a minimum when the atomic orbitals—components of molecular orbitals—have equal energy (degeneration).

For $H_2^+$ the coefficient $C$ becomes equal to $\pm 1$ and two functions* are obtained from the above cited equation:

$$\psi_g = \psi_{(a:1s)} + \psi_{(b:1s)}$$

$$\psi_u = \psi_{(a:1s)} - \psi_{(b:1s)}$$

Linear combination of the atoms' eigenfunctions again leads to two solutions with two different values for the energy. Of these solutions only one describes the attractive state, the other refers to the repulsive state. The difference in the energy of these two states is described by the resonance integral $\beta$, which corresponds to integral $I$ of the valence bond method. The resonance integral

* The subscript $g$ in $\psi_g$ indicates an "even" subscript, and the subscript $u$ in $\psi_u$—an "odd" one.

is negative, and therefore $E = E_a + \beta$ corresponds to the attractive, and $E = E_a - \beta$ to the repulsive state of the electron in question. It is important to know the electronic states of the two electrons participating in the formation of the atomic bond.

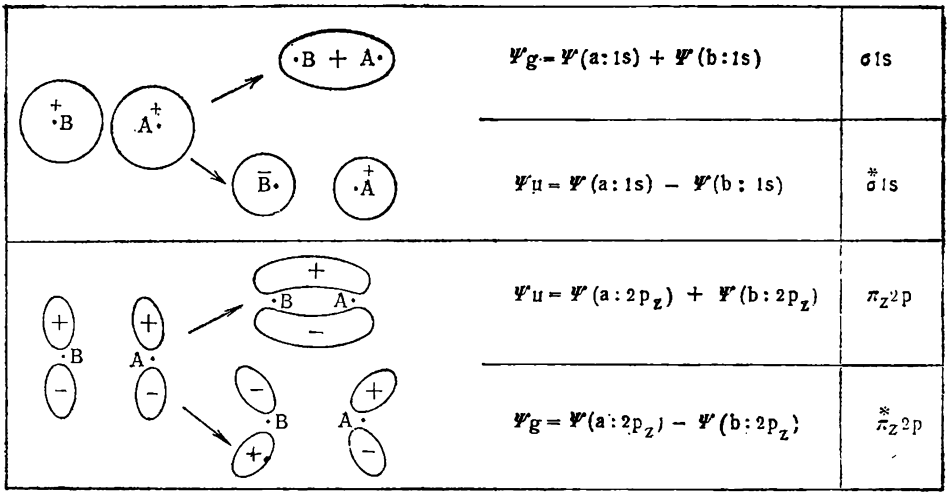



FIGURE 1-7 Bonding and nonbonding $\sigma\sigma$ * and $\pi\pi$ * molecular orbitals and their formation from atomic orbitals

Figure 1-7 [51] illustrates the outlines of the bonding ($\sigma$ and $\pi$) and nonbonding ($\sigma^*$ and $\pi^*$) molecular orbitals, forming from atomic orbitals (for the combination of two $s$ and two $p_x$ or, respectively, two $p_y$ or two $p_z$ electronic states)[1].

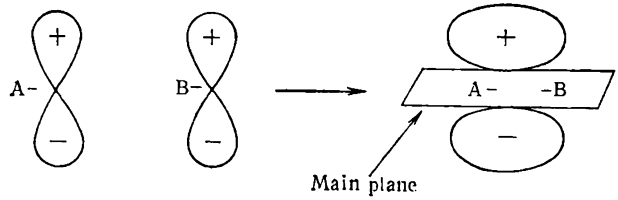



FIGURE 1-8 Formation of the bonding $\pi$ molecular orbital

The formation of the bonding $\pi$ molecular orbital from two $p_y$ or two $p_z$ orbitals is better represented, as in Figure 1-8.

The plane $AB$ is the main plane, the total is the "molecular orbital" of two $p_y$ or two $p_z$ electrons (exchange of the combination

[1] The signs + and — signify the sign of $\psi$ (it does not affect the physical meaning of $\psi^2$).

of two $p_y$ orbitals for two $p_z$ orbitals gives the same pattern of the $\pi$ molecular orbital, but rotated through 90°).

Molecular orbitals may be classified:

(1) according to their symmetry with respect to the molecular axis;

(2) according to their bonding or nonbonding character;

(3) according to the atomic eigenfunctions into which the molecular eigenfunctions decompose when the internuclear distances are large.

Molecular orbitals possessing cylindrical symmetry with regard to the molecular axis are called $\sigma$ orbitals. Molecular orbitals, forming as a result of the combination of $p_y$ or $p_z$ atomic eigenfunctions are called $\pi$ orbitals and are designated $\pi_y$ or $\pi_z$.

Above (pages 40-41) we considered the description of atomic eigenfunctions with the aid of the principal, orbital, magnetic and spin quantum numbers. This method of description applies also for molecular orbits, $n$ and $l$ having the same meaning. The magnetic quantum number has a different meaning here and is therefore designated otherwise ($\lambda$ instead of $m$). The direction of the magnetic quantum number is determined in this case with regard to the axis. Molecular orbitals with $\lambda = 0$ are symmetrical with regard to the $A - B$ axis (these are $\sigma$ orbitals). For $\pi$ orbitals $\lambda = \pm 1$, for $\delta$ orbitals $\lambda = \pm 2$.

The $\sigma$ orbitals are not degenerate; other types of orbitals are characterized by double degeneration corresponding to a component with electronic motion around $A - B$ in the positive or negative direction.

The second possibility of classification corresponds to the two solutions of the wave equation by the method of linear combinations of atomic eigenfunctions. The antibonding state is designated by a Greek letter with an asterisk, for example, $\sigma^*$ or $\pi^*$. Besides, $\sigma$ and $\pi$ correspond to the symmetrical, and $\sigma^*$ and $\pi^*$, to the antisymmetrical function; the first case is also called even ($\psi_g$) and the second odd ($\psi_u$) if bonds between similar atoms are considered.

The third method of classification makes it possible to establish what atomic eigenfunctions the molecular eigenfunction is composed of or which atomic orbitals a molecular orbital reduces to when the distance between the nuclei is large.

Therefore, molecular orbitals formed from $1s$ orbitals are also designated $\sigma 1s$ or $\sigma^* 1s$ or $\pi_z 2p$ or $\pi_z^* 2p$, respectively. The $\sigma$ orbital consisting of two $s$ orbitals (for instance, in the H — H bond) is designated $\sigma^2$ orbital for short.

Various electron levels are filled with electrons in turn in the order of increasing energy. For molecules composed of atoms of

the second row of the Periodic System this order is as follows (the energy values of the $\sigma 2p$ and $\pi 2p$ orbitals are very close):

$$\sigma 1s < \sigma^* 1s < \sigma 2s < \sigma^* 2s < \sigma 2\pi < \pi_y 2p = \pi_z 2p < \pi_y^* 2p = \pi_z^* 2p < \sigma^* 2p \quad (1)$$

There is still another method of abbreviated designation of molecular orbits, which may be demonstrated for $Li_2$ and $Na_2$ by way of example. In relatively heavy atoms (like Li or Na) the designation of inner electron orbitals which do not participate in the formation of an atomic bond, for example $(\sigma 1s)^2\ (\sigma^* 1s)^2$, is changed to the designation $KK$, which indicates completion of both $K$ shells.

$$Li_2 = Li\ (1s^2 2s) + Li\ (1s^2 2s) \longrightarrow Li\ [KK\ (\sigma 2s)^2]$$

Similarly the $L$-shell of $Na_2$:

$$Na_2 = [KKLL\ (\sigma 3s)^2]$$

If the molecular orbital is already occupied by two electrons, then the approach of a third electron with a similar atomic eigenfunction results in repulsion. This is due to the saturation of valence.

Molecular orbitals follow Pauli's principle, limiting the number of possible electrons in each molecular orbital. The $\sigma$ and $\sigma^*$ states accommodate two electrons each, and each of the $\pi$ and $\pi^*$ states, four electrons (two electrons in the $\lambda = +1$ orbital and two in the $\lambda = -1$ orbital).

The MO method gives approximate solutions, because to simplify the calculation, excitation of atomic eigenfunctions by other atoms is not taken into consideration. For a diatomic molecule $\psi = C_a\psi_a + C_b\psi_b$. When two electrons are present, each of them is described by a function of the above-mentioned type; thus, according to MO method the following equation results for a hydrogen molecule (in case of like atoms $C_a = C_b$ and it may be given the value of 1):

$$\psi = [\psi_a(1) + \psi_b(1)] \cdot [\psi_a(2) + \psi_b(2)] = \psi_a(1) \cdot \psi_b(2) + \psi_a(2) \cdot \psi_b(1) + \psi_a(1) \cdot \psi_a(2) + \psi_b(1) \cdot \psi_b \quad (2)$$

Comparing this equation with that obtained for the hydrogen molecule by the valence bond method, it is apparent that besides two members characteristic of the homopolar bond, two ionic members appear in the wave equation, due to the $H^-H^+$ and $H^+H^-$ states. It should be noted that such a calculation involves a definite disadvantage alongside the advantage of calculating ionic states,

viz.: all the terms of the wave function are assigned the same weight. This is due to the fact that in the MO method the ionic conditions are overestimated. Application of the MO method to polyatomic molecules is very difficult. In some cases these difficulties may be overcome by making an additional assumption concerning localized molecular orbitals; in other cases, for example, in excited states or in systems with conjugated bonds, approximate calculation is possible only if non-localized molecular orbitals are utilized. Localized molecular orbitals (in case of $\pi$ bonds) are possible only between two nuclei. Non-localized $\pi$ bonds arise in cases where several nuclei are present (for example, the benzene molecule has six $\pi$ electrons in a field of six nuclei). Besides, the $\pi$ electrons are not grouped in pairs between two C atoms, but constitute a common molecular orbital encompassing all six carbon atoms.

In spite of certain difficulties, application of the MO method to the calculation of polyatomic molecules is already producing important results.

The characteristics of $\pi$ electron systems—total energies of $\pi$ electrons, energies of individual molecular orbitals, excitation energies, etc., have been obtained for a large number of molecules. Thus, for the $6\pi$ electrons in benzene calculation results in six molecular orbitals

$$C_1\psi_1+C_2\psi_2+C_3\psi_3+\ldots+C_6\psi_6$$

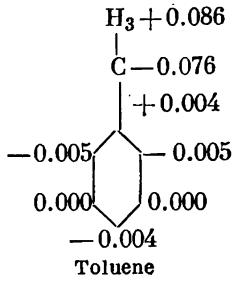
where $C = \int \psi_i H \psi_i \, d\tau$, $\beta = \int \psi_i H \psi_j \, d\tau$; $i$ and $j$ being neighbouring atoms, H is Hamilton's operator, including the kinetic energy of the $\pi$ electron and its interaction with all the nuclei and the other electrons.

In the ground state of the benzene molecule the $6\pi$ electrons occupy three lower orbitals in pairs. The total energy of these electrons equals $6C + 8\beta$, while the energy of an isolated $\pi$ bond (2 electrons on the bicentral MO $\psi_1 + \psi_2$ with energy $C + \beta$) equals $2C + 2\beta$, and the energy of three such isolated bonds, $6C + 6\beta$. Apparently, the presence of electrons in the field of all the six carbon atoms results in an energy gain of $2\beta$.

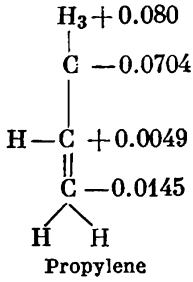
The MO method gives an idea of the distribution of $\pi$ electron density in the molecule. The so-called molecular diagrams of many molecules have now been calculated, indicating the electronic or effective charges which characterize the relative electron density around a given atom, the orders of the bonds and indices of free valence of atoms, reflecting the degree of unsaturation.

Given below are the diagrams obtained for toluene, propylene, aniline, chlorobenzene and pyridine (the numbers indicate the

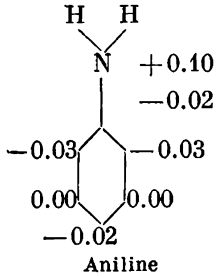
electronic or effective charges of the atoms, characterizing the relative electron density around each given atom*).



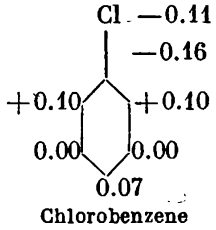
Toluene



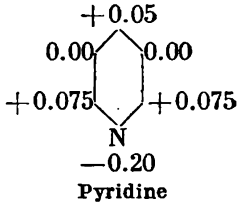
Propylene



Aniline



Chlorobenzene



Pyridine

An evaluation of the relative activity of molecules with conjugated bonds and of molecules of aromatic compounds in reactions with free radicals was carried out with the aid of the MO method.

The starting point is the assumption that in these reactions the least saturated atoms are the most active. In connection with this the quantity "index of free valence" ($F$) was introduced, characterizing the "degree of unsaturation" of a given atom (similar to some extent to the "partial valence" of Thiele).

The index of free valence, $F$, is determined as follows. It is assumed that the order of the carbon-carbon bond** equals 1 in ethane,

* To calculate the electron charges in compounds of the type of toluene and propylene the "pseudoatom $H_3$" and the carbon of the methyl group linked to it are regarded as $\pi$-electron donors. Thus, in calculating the propylene molecule, for instance, four $\pi$ electrons are used rather than two. The diagrams of electronic charge distribution in the molecules of aniline, chlorobenzene, and pyridine show the effective charges dependent only on the $\pi$ electrons distribution. On this distribution is superimposed the inductive shift of $\sigma$ electrons, caused by the presence of a substituent (or a heteroatom). This shift results in the appearance at the substituent (or heteroatom) and at the carbon atom directly linked to it of an effective charge, whose absolute value is, apparently, generally larger than the effective charge caused by the distribution of $\pi$ electrons. The charge of more remote carbon atoms is determined mainly by the distribution of $\pi$ electrons alone, because inductive influence damps rapidly along a chain of atoms.

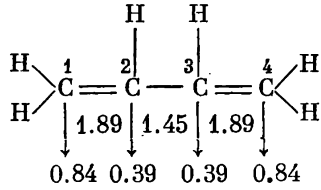
** "Bond order" is a quantity characterizing the degree of deviation of a given bond from a single bond and approximately proportional to the electron density at the midpoint between two directly linked atoms.

2 in ethylene, and 3 in acetylene. The C — C bonds in conjugated and aromatic systems will then have fractional orders.

On the basis of the concept of bond order a special quantity $N$, the degree of bonding (degree of unsaturation) of atom, is introduced. $N$ is defined as the sum of the orders of all the bonds of a given atom (the order of the C—H bond being taken as 1).

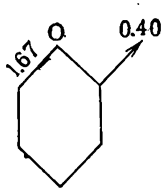
The maximum degree of bonding possible for carbon (calculated theoretically) $N_{max} = 4.73$. If we subtract the value of $N$ of a given carbon atom from its maximum value $N_{max}$ we get the index of free valence $F$ ($F = N_{max} - N$).

Cited below are the bond orders and indices of free valence (indicated by arrows) of the carbon atoms in the butadiene molecule, calculated by the MO method.

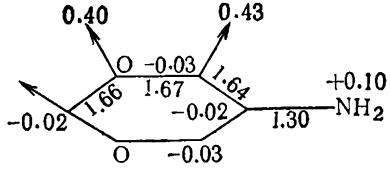



For the first carbon atom $F_1 = 0.84$, for the second $F_2 = 0.39$. Therefore, radicals should add easier to the first than to the second atom.

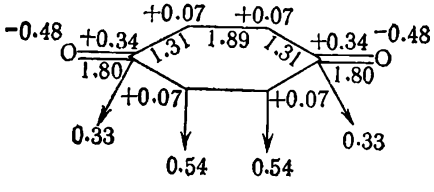
The bond orders and indices of free valence have been calculated by the MO method for many aromatic compounds. The molecular diagrams of benzene, aniline, benzoquinone, naphthalene and quinoline are given below by way of example:



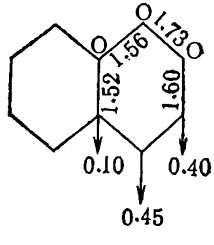

Benzene



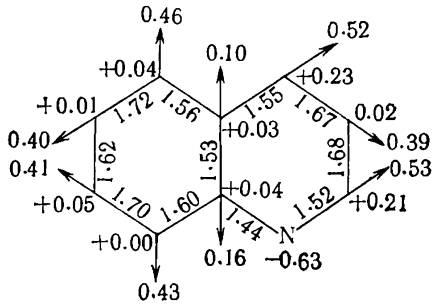

Aniline




Benzoquinone




Naphthalene




Quinoline

Diagrams of this type may be of great importance in predicting and explaining the reactivities of organic compounds.

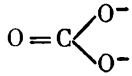
Despite the great complexity of the mathematical apparatus the method of molecular orbitals is rapidly gaining a dominant position among approximate quantum-mechanical methods of calculation [53, 54, 55, 56].

Recently calculations of σ-electron density distribution in saturated compounds have been carried out [57].

### Methods of Depicting Electron Density Distribution in Molecules

As indicated on page 67 for the example of the benzene molecule, classical structural formulas of aromatic compounds and aliphatic compounds with conjugated bonds, while correctly representing the sequence of atomic linkages (chemical structure) are inadequate in one respect: these formulas do not reflect the true distribution of electron density.

For example, it follows from the classical formula of the carbonate anion that two equivalent

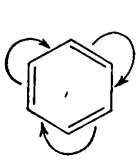


atoms of oxygen carrying negative charges are linked by single bonds to a carbon atom, and that the neutral oxygen atom is linked to it with a double bond. Actually, all three oxygen atoms in the carbonate anion are equivalent: all the three interatomic C — O distances are equal, and the two negative charges are equally distributed among the three oxygen atoms.

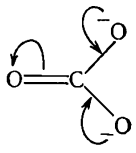
At present three methods of depicting electron densities in molecules are most widely used.

The first method consists essentially in correcting the classical structural formulas by bent arrows indicating the direction of shift of the electrons (with respect to the electron density distribution given by the classical structural formula). The carbonyl

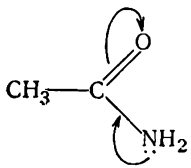
group is portrayed by this method on page 46; below are the formulas of benzene, carbonate ion, acetamide and acrolein.



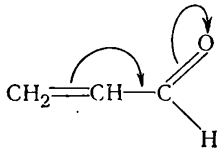
Benzene



Carbonate ion



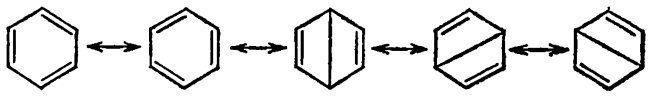
Acetamide



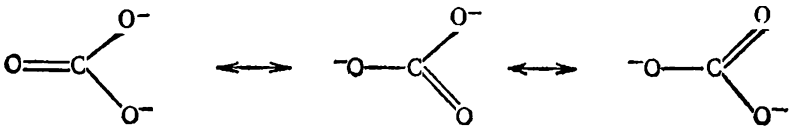
Acrolein

This method is convenient in the majority of cases, as its wide use in the chemical literature shows. However, this method has its faults. First of all, it is inconvenient because the same bent arrows indicate electron shifts at the moment of reaction (electromeric shifts), and sometimes the sum of both static and dynamic effects. Besides, quantitatively unequal electronic shifts are not differentiated by this method.

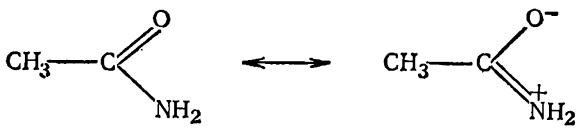
The second possible method of showing the distribution of electron density in molecules consists in writing several classical structural formulas for a given molecule (with double-pointed arrows between the structures); it is understood that the true structure of the molecule is intermediate, "hybrid", between the "limiting structures" indicated and is described by their totality, for example:



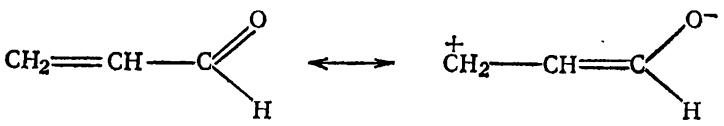
Benzene



Carbonate ion

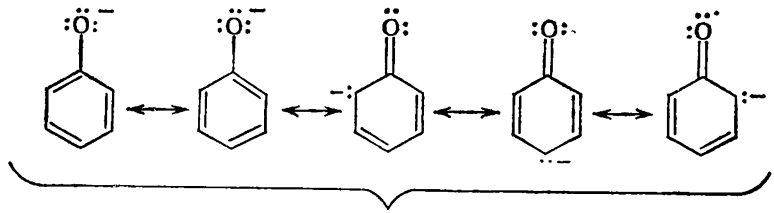


Acetamide



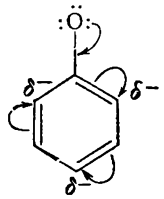
Acrolein

The polystructural method of depicting electron density distribution in molecules is less convenient than other suggested methods in the majority of cases. For example, according to this method the formula (I) of phenolate ion is represented by a set of five limiting structures

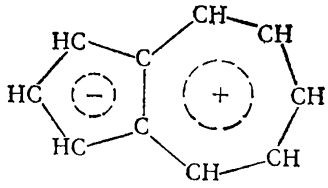


I

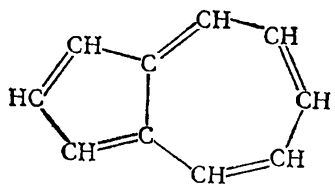
while it can be written much more conveniently using the bent-arrow method:



However, examples may be cited, where the polystructural method of formula writing is apparently more descriptive. If we write the two structures for the azulene molecule, viz., bipolar (A) and classical (B), the simplest way of imagining the structure of this molecule is apparently as an intermediate between the two limiting structures:



A

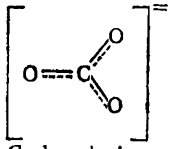


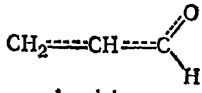
B

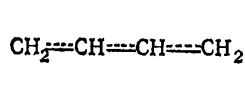
It would be very complicated to portray the structure of azulene by a formula like that of phenolate ion with the aid of bent arrows.

In the polystructural method of writing formulas it is sometimes possible to give an idea of the magnitude of electronic shift by indicating for each structure the coefficient calculated for the function $\psi_n$ by the electronic pair method. However, it should be kept in mind that the more complex the molecule, the less reliable are such calculations.

Finally, a third possible method of depicting the distribution of electronic density in conjugated aliphatic systems and aromatic molecules consists in using dotted lines to reflect equalization of bonds, for example:

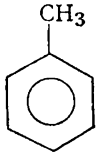

Carbonate ion

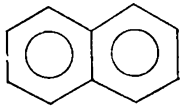

Acrolein

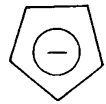

Butadiene

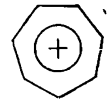
Benzene

To portray aromatic systems solid lines are currently employed rather than dotted lines, for example:


Toluene

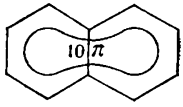

Naphthalene


Cyclopentadienylium anion


Tropylium cation

Sometimes in the formulas of this type the number of jointly shared $\pi$ electrons is indicated, and in condensed aromatic systems common rather than separate circles are used to symbolize common $\pi$-electron clouds, e.g.:

Benzene


Naphthalene

Anthracene

Currently the third of these methods for representing electron density distribution is gaining favour rapidly because of its vividness.

### Acidic and Basic Properties of Organic Compounds

According to the classical definition (Arrhenius), *bases* are compounds which yield hydroxide ions when dissolved in water, while *acids* are compounds which produce hydrogen ions. Thus, the terms base and acid referred originally only to reactions taking place in aqueous media.

However, the concept of acidic and basic properties of substances became so useful and important that numerous attempts were made to revise the above definitions and define acids and bases more generally [60, 61, 62].

The most important of these for organic chemistry are the concepts of Brönsted and of Lewis.

**Theory of Protolytic Acid-Base Equilibrium (Brönsted's Theory).** According to Brönsted, *acids* are substances which yield protons, and *bases*—substances which gain protons.

Brönsted points out the analogy between the oxidation-reduction and acid-base reactions.

In oxidation-reduction reactions an electron migrates from the reducing agent to the oxidizing agent, while in acid-base reactions the acid gives up a proton to the base.

Having lost an electron, the reducing agent becomes an oxidizing agent; when an acid has donated a proton, it becomes a base.

Thus, according to Brönsted classical acids are also acids

$$\left.\begin{aligned} H_2SO_4 &\longrightarrow H^+ + HSO_4^- \\ HCOOH &\longrightarrow H^+ + HCOO^- \\ C_6H_5OH &\longrightarrow H^+ + C_6H_5O^- \end{aligned}\right\} \textit{Conjugate bases}$$

The anions ($HSO_4^-$, $HCOO^-$, $C_6H_5O^-$), formed as a result of the removal of protons from the acid molecules, are called the *conjugate bases* of the corresponding acids.

Though Brönsted's definition of acids is very similar to the classical definition, the Brönsted acids include a large number of acids which are not acids in the classical sense, for example:

$$CH_3{-}NO_2 \longrightarrow H^+ + [CH_2{-}NO_2]^-$$

$$(CH_3)_3\overset{+}{N}H \longrightarrow H^+ + (CH_3)_3N$$

$$Al(H_2O)_6^{+++} \longrightarrow H^+ + [Al(H_2O)_5OH]^{++}$$

Dissociations of this type do not occur spontaneously, but only under the influence of bases.

Brönsted's bases are substances which gain protons; generally they are negative ions or neutral molecules, but there are a few cases, for example $[Zn(H_2O)_3OH]^+$, where bases are positively charged ions.

Examples of Brönsted's bases are given below:

$$\left.\begin{aligned} &OH^- + H^+ \longrightarrow H_2O \\ &CO_3^{=} + H^+ \longrightarrow HCO_3^- \\ &\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!O + H^+ \longrightarrow \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!\overset{+}{O}{-}H \\ &CH_3O^- + H^+ \longrightarrow CH_3OH \\ &C_6H_5{-}NH_2 + H^+ \longrightarrow C_6H_5\overset{+}{N}H_3 \\ &CH_3COOH + H^+ \longrightarrow \left[CH_3{-}C\begin{matrix}OH\\OH\end{matrix}\right]^+ \end{aligned}\right\} \textit{Conjugate acids}$$

Ions and molecules which form as a result of the addition of protons to bases are called *conjugate acids* of those bases.

A complete acid-base reaction comprises a proton transfer from acid to base, for example:

TABLE 1-1

| Acid | | Base | | Conjugate acid | | Conjugate base |
|---|---|---|---|---|---|---|
| $H_3O^+$ | $\rightleftharpoons$ | $OH^-$ | $\rightleftarrows$ | $H_2O$ | $\rightleftharpoons$ | $H_2O$ |
| $H_2O$ | $\rightleftharpoons$ | $H^-$ | $\rightleftarrows$ | $OH^-$ | $\rightleftharpoons$ | $H_2$ |
| $H_2SO_4$ | $+$ | $H_2O$ | $\rightleftarrows$ | $HSO_4^-$ | $+$ | $H_3O^+$ |
| HCOOH | $\rightleftharpoons$ | $HCO_3^-$ | $\rightleftarrows$ | $HCOO^-$ | $\rightleftharpoons$ | $H_2CO_3$ |
| $H_2O$ | $+$ | $H_2O$ | $\rightleftarrows$ | $OH^-$ | $\rightleftharpoons$ | $H_3O^+$ |

It is apparent from Table 1-1 that water, like many other hydroxyl-containing substances, may be either an acid or a base; water molecules may lose or gain protons depending on the presence in it of basic or acid substances.

"Autoionization" reactions, like reactions of autoprotolysis of water, are more or less possible in other polar solvents as well. They result in equal amounts of *lyonium ions* (conjugate acid of the solvent) and *lyate ions* (conjugate base of the solvent), for example, in the cases of methanol and formic acid:

$$2CH_3OH \longrightarrow CH_3-\overset{+}{O}\begin{matrix}H\\H\end{matrix} + CH_3O^-; \quad K=(CH_3\overset{+}{O}H)_2(CH_3O^-)=2\times10^{-17}$$

$$2HCOOH \longrightarrow \left[H-C\begin{matrix}OH\\OH\end{matrix}\right]^+ + HCOO^-; \quad K=(HCOOH_2^+)(HCOO^-)=6\times10^{-17}$$

According to Brönsted's concepts, very strong acids must be very weak conjugate bases and, conversely, strong bases should be weak conjugate acids. Thus, if the acid HX is stronger than the acid HY, the base $Y^-$ will be stronger than the base $X^-$.

**Types of Solvents.** Above we gave examples of reactions illustrating the amphoteric properties of water. The amphoterity of water is due to the fact that one molecule performs the function of a base and another, of an acid.

Amphoteric solvents (say, water or alcohols) are called *amphiprotic.*

Solvents (such as benzene, cyclohexane and chlorobenzene), the molecules of which are incapable of either giving or accepting protons, are called *aprotic.*

Solvents of a basic nature, the molecules of which possess a great affinity for protons (liquid ammonia, amines, pyridine) are called *protophilic.*

Solvents of an acid nature, the molecules of which part readily with a proton (anhydrous formic acid, anhydrous sulphuric acid, liquid hydrogen fluoride), are called *protogenic.*

It should, however, be taken into consideration that even solvents with predominantly basic or acidic properties generally exhibit amphoteric properties too, for example:

| | Acid | Base | | Conjugate acid (lyonium ions) | Conjugate base (lyate ions) |
|---|---|---|---|---|---|
| Protogenic | $H_2SO_4$ | $+H_2SO_4$ | $\rightleftarrows$ | $H_3SO_4^+$ | $+HSO_4^-$ |
| | HCOOH | +HCOOH | $\rightleftarrows$ | $HCOOH_2^+$ | $+HCOO^-$ |
| | $CH_3COOH$ | $+CH_3COOH$ | $\rightleftarrows$ | $CH_3COOH_2^+$ | $+CH_3COO^-$ |
| Amphitropic | $H_2O$ | $+H_2O$ | $\rightleftarrows$ | $H_3O^+$ | $+OH^-$ |
| | $CH_3OH$ | $+CH_3OH$ | $\rightleftarrows$ | $CH_3OH_2^+$ | $+CH_3O^-$ |
| | $C_2H_5OH$ | $+C_2H_5OH$ | $\rightleftarrows$ | $C_2H_5OH_2^+$ | $+C_2H_5O^-$ |
| Protophilic | $HCONH_2$ | $+HCONH_2$ | $\rightleftarrows$ | $HCONH_3^+$ | $+HCONH^-$ |
| | $NH_2—NH_2$ | $+NH_2—NH_2$ | $\rightleftarrows$ | $NH_2—NH_3^+$ | $+NH_2—NH^-$ |
| | $NH_3$ | $+NH_3$ | $\rightleftarrows$ | $NH_4^+$ | $+NH_2^-$ |

The positions of equilibrium in the above ionization reactions of solvents of various types may be characterized by autoprotolysis constants (product of lyonium and lyate ion concentrations).

The autoprotolysis constants of a number of solvents (at 25°) are listed below (Table 1-2).

TABLE 1-2

**Autoprotolysis Constants of Some Solvents**

| Solvent | *K* | Solvent | *K* |
|---|---|---|---|
| Sulphuric acid | $1 \times 10^{-5}$ | Ethanol | $8 \times 10^{-20}$ |
| Formic acid | $5 \times 10^{-7}$ | Formamide | $1 \times 10^{-17}$ |
| Acetic acid | $2.5 \times 10^{-13}$ | Hydrazine | $2 \times 10^{-25}$ |
| Water | $1 \times 10^{-14}$ | Ammonia | $3 \times 10^{-33}$ |
| Methanol | $2 \times 10^{-17}$ | | |

**Effect of Solvents on the Strength of Acids and Bases.** When we speak of complete ionization of an acid HA in the solvent S we mean that the molecules of the acid reacted completely with the molecules of the solvent:

$$HA + S \longrightarrow HS^+ + A^-$$

Thus, the observed acid strength depends on the proton-acceptor ability of the solvent, or, in other words, on the basic properties of the solvent. Thus, carboxylic acids, with a few exceptions, are weak acids in water, but they ionize completely when dissolved in liquid ammonia, because their reaction with this basic solvent is practically complete:

$$R—COOH + NH_3 \longrightarrow NH_4^+ + RCOO^-$$

Liquid ammonia, because of its basic properties, has a "levelling effect" on the strength of acids dissolved in it: all carboxylic acids dissolved in liquid ammonia are ionized to the same extent and appear to be as strongly acidic as mineral acids.

To differentiate the strength of acids, solvents of a less basic nature must be selected.

The use of water as the solvent makes it clear that mineral acids are stronger than carboxylic acids.

To decide which of the mineral acids are stronger and which weaker, use should be made of solvents possessing still weaker basic properties than water or having a lower ionizing ability or combining both of these properties.

For example, in methanol, nitric acid is only partially ionized while hydrogen chloride is fully ionized; in anhydrous formic acid hydrogen chloride is partially, but sulphuric acid is fully ionized 64].

$$HNO_3 + CH_3OH \rightleftarrows CH_3OH_2^+ + NO_3^-$$

$$HCl + CH_3OH \longrightarrow CH_3OH_2^+ + Cl^-$$

$$HCl + HCOOH \rightleftarrows HCOOH_2^+ + Cl^-$$

$$H_2SO_4 + HCOOH \longrightarrow HCOOH_2^+ + HSO_4^-$$

In glacial acetic acid the dissociation constant of $HClO_4$ equals $1.6 \times 10^{-4}$, HBr — $4 \times 10^{-5}$, $H_2SO_4$ — $6 \times 10^{-7}$, HCl — $1.4 \times \times 10^{-7}$, $HNO_3$ — $4.2 \times 10^{-8}$, $CCl_3COOH$ — $2.3 \times 10^{-10}$ (after Izmailov [65]).

From a comparison of a series of different acids in the same solvent it follows that the strongest acid is the one which is ionized to the greatest extent. A study of the acidity of solutions of the same acid in different solvents shows that the most acid solution is the one in

which the acid is the least ionized. This can be explained using as examples aqueous and benzene solutions of hydrogen chloride. In water, hydrogen chloride exists predominantly as $H_3O^+$ and $Cl^-$ ions, that is, as the products of neutralization of HCl by water. In benzene HCl is practically unionized.

If the same indicator is used in both solutions, it will show a greater acidity in the benzene solution of hydrogen chloride. This is due to the fact that in the process of proton addition (and its conversion to a conjugate acid) the indicator molecules, in the case of an aqueous solution, have to compete with $H_2O$ molecules, while in the case of benzene solution they have the much less basic $Cl^-$ anions to compete with. Thus, a benzene solution of hydrogen chloride is a better donor of protons than an aqueous solution.

The ionization constants of some acids and bases in water (at 25°) are given below:

| *Acids* | | *Bases* | |
|---|---|---|---|
| $H_3PO_4$ | $7.6 \times 10^{-3}$ | Guanidine | $3 \times 10^{-1}$ |
| $H_3BO_3$ | $5.8 \times 10^{-10}$ | Piperidine | $1.6 \times 10^{-3}$ |
| $H_2CO_3$ | $3.5 \times 10^{-7}$ | Triethylamine | $6 \times 10^{-4}$ |
| $H_2S$ | $5.7 \times 10^{-8}$ | Ammonia | $1.7 \times 10^{-5}$ |
| HCOOH | $2.1 \times 10^{-4}$ | Hydrazine | $8.5 \times 10^{-7}$ |
| $CH_3COOH$ | $1.8 \times 10^{-5}$ | Pyridine | $2.3 \times 10^{-9}$ |
| $C_6H_5COOH$ | $6 \times 10^{-5}$ | Aniline | $3 \times 10^{-10}$ |
| $CCl_3COOH$ | $3 \times 10^{-1}$ | Urea | $1.5 \times 10^{-14}$ |
| HCN | $7.2 \times 10^{-10}$ | Acetamide | $3.1 \times 10^{-15}$ |

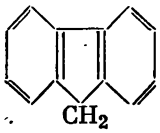
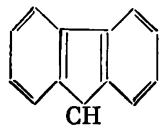
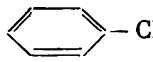
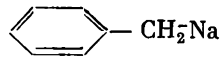
**Very Weak Acids.** Organic compounds include very weak acids: even when dissolved in liquid ammonia they are ionized to an immeasurably small degree.

It is apparent that to remove a proton from such substances a much stronger base than ammonia is required. Such a base, for example, is hydroxyl ion $OH^-$; but even its basicity is not strong enough to convert weak acids into conjugate bases. This limits the possibility of ionization of very weak acids in water solutions, because if an attempt were made to use a base B stronger than hydroxyl ion this base would immediately react with water to form $OH^-$ ions:

$$B + H_2O \longrightarrow BH^+ + OH^-$$

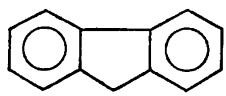
Ionization of many weak acids and their attendant transformation into conjugate bases (alcohols, amines, certain hydrocarbons) was achieved by the action of amide ion, $NH_2^-$, in liquid ammonia. Transformation of substances of acids still weaker than ammonia into their conjugate bases may be achieved in ether or hydrocarbon media.

Several examples of the transformation of very weak Brönsted acids into their conjugate bases may be cited.

| | Acid | | Base | | Conjugate base | | Conjugate acid |
|---|---|---|---|---|---|---|---|
| (1) | $CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-OH$ | + | $NH_2^-$ | → | $CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-O^-$ | + | $NH_3$ |
| (2) |  | + | $NH_2^-$ | → |  | + | $NH_3$ |
| (3) | $Ph_2NH$ | + | $Ph_3\overset{(-)}{C}:$ | → | $Ph_2\overset{(-)}{N}:$ | + | $Ph_3CH$ |
| (4) |  | + | PhNa | → |  | + | PhH |

Ionization of *tert*-butanol and indene under the influence of the amide ion [reactions (1) and (2)], and of diphenylamine by the action of the triphenylmethyl anion [reaction (3)] can be effected in liquid ammonia or in ether [66] and proton transfer from the methyl group of toluene to the phenyl anion of phenylsodium can be carried out in hydrocarbon solvents [67].

The ionization constants of some very weak acids (with water conventionally as the solvent) are as follows:

| | | |
|---|---|---|
| Methanol | $CH_3OH$ | $10^{-16}$ |
| Acetophenone | $PhCOCH_3$ | $10^{-19}$ |
| Phenylacetylene | $PhC \equiv CH$ | $10^{-23}$ |
| Fluorene |  | $10^{-25}$ |
| Triphenylmethane | $Ph_3CH$ | $10^{-33}$ |
| Diphenylmethane | $Ph_2CH_2$ | $10^{-35}$ |
| Cumene | $PhCH(CH_3)_2$ | $10^{-37}$ |
| Ethane | $CH_3-CH_3$ | $10^{-40}$ |

**Very Weak Bases.** If organic compounds were arranged in a series according to their acid-base properties, the end opposite from the very weak acids would contain the very weak bases such as esters, carboxylic acids, amides, ketones, nitro compounds and certain aromatic hydrocarbons.

Although some of these compounds are slightly soluble in water, their basicities cannot be studied in aqueous solutions: addition of a strong acid to the aqueous solution of these substances leads to the same result—almost exclusively to the formation of hydroxonium ion, $H_3O^+$ which is the conjugate acid of water. As simultaneously only insignificant amounts of conjugate acids of very weak organic bases are formed, other means of detecting the basicity of the latter must be sought.

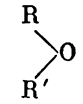
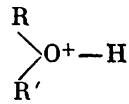
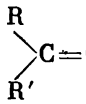
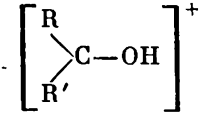
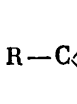
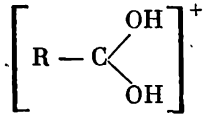
The most widely used solvent for this purpose is 95-100% sulphuric acid, and the most useful method, cryoscopy.

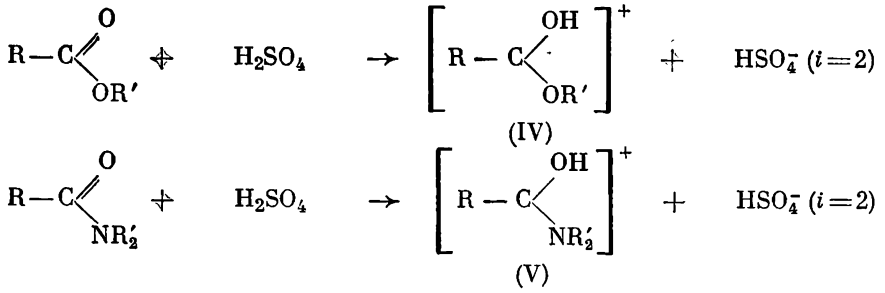
In this type of investigations [68] the experimentally observed lowering of the freezing point is compared with the depression due to the undissociated dissolved substance at the same concentration. The number of particles formed upon the solution of one molecule of the substance ($i$-factor) is calculated from the ratio of the two depression values found.

Thus, in the case of trifluoroacetic and chloric acids, which exhibit neither acid nor base type ionization in sulphuric acid, the factor $i$ is close to unity. On the other hand, for compounds which behave like monoacidic bases in sulphuric acid the factor $i$ equals 2.

$$B + H_2SO_4 \rightarrow HB^+ + HSO_4^- \ (i = 2)$$

Compounds of this type include monoacidic amines, ethers which form oxonium compounds of the type $R_2\overset{+}{O}H$ (I), ketones, monocarboxylic acids, their esters and amides transforming into cations of types II-V:

| Base | Acid | Conjugate acid | Conjugate base |
|---|---|---|---|
|  | $H_2SO_4$ |  (I) | $HSO_4^-$ $(i=2)$ |
|  | $H_2SO_4$ |  (II) | $HSO_4^-$ $(i=2)$ |
|  | $H_2SO_4$ |  (III) | $HSO_4^-$ $(i=2)$ |



(IV)



(V)

The values of the *i*-factors of nitro compounds, cyclic anhydrides of dicarboxylic acids and sulphoacids vary between 1 and 2. It follows that in sulphuric acid solution these compounds are not fully converted into their conjugate acids [69].

Benzene and its homologues are almost insoluble in sulphuric acid, but they dissolve in hydrofluoric acid yielding solutions which conduct electric current [70]. This indicates that benzene and its homologues behave like bases in reactions with HF.

$$ArH + 2HF \longrightarrow ArH_2^+ + HF_2^-$$

When a solution of ArH in HF is diluted with water, the hydrocarbon separates out in the free state.

The basic nature of benzene was established also by another method: benzene enters into a deuteroexchange reaction with $D_2SO_4$ [71]. This exchange most probably proceeds through the stage of the intermediate cation $C_6H_6D^+$:

$$C_6H_6 + D_2SO_4 \rightleftarrows [C_6H_6D]^+ \rightleftarrows C_6H_5D + DHSO_4$$

An analogous exchange takes place with deuterium fluoride DF [72].

**Influence of Dielectric Constant on Position of Acid-Base Equilibrium.** Thus, the acid-base properties of a chemical compound depend greatly, besides its structure, on the nature of the solvent (more precisely, on the relative proton affinity of the substance and the solvent).

One and the same substance may ionize as an acid or as a base in different solvents.

For example, aniline in water is a base, but in liquid ammonia it is a weak acid; acetic acid is an acid in water, but a base in sulphuric acid:

| Base | Acid | | Conjugate acid | Conjugate base |
|---|---|---|---|---|
| $Ph—NH_2$ | $+ H_2O$ | $\rightleftarrows$ | $Ph—\overset{+}{N}H_3$ | $+ OH^-$ |
| $NH_3$ | $+ Ph—NH_2$ | $\rightleftarrows$ | $NH_4^+$ | $+ PhNH^-$ |
| $H_2O$ | $+ CH_3COOH$ | $\rightleftarrows$ | $H_3O^+$ | $+ CH_3COO^-$ |
| $CH_3COOH$ | $+ H_2SO_4$ | $\rightleftarrows$ | $CH_3COOH_2^+$ | $+ HSO_4^-$ |

The value of the dielectric constant of the solvent should have a substantial influence on the establishment of acid-base equilibria.

TABLE 1-3

**Dielectric Constants of Some Solvents**

| | | | |
|---|---|---|---|
| Hydrocyanic acid | 123 (15.6°) | Acetone | 22 |
| Formamide | 110 | Ammonia | 17 |
| Sulphuric acid | 110 (20°) | Pyridine | 12 |
| Hydrogen fluoride | 84 | Aniline | 7.2 |
| Water | 79 | Acetic acid | 7.1 |
| Hydrazine | 54 | Ethyl ether | 4.5 |
| Formic acid | 50 | Benzene | 2.3 |
| Methanol | 31.5 | Chlorobenzene | 5.8 |
| Ethanol | 24.2 | *n*-Pentane | 1.8 |

These values may serve as a crude measure of the relative abilities of solvents to facilitate the separation of positive and negative ions in solutions.

It is apparent from the table that the dielectric constant of water is approximately 50% higher than that of formic acid, much higher than that of alcohol, 10 times higher than that of acetic acid and many times higher than that of ether and benzene. This means that association of ions, which is observed in water only at high concentrations of the dissolved substances, will occur even in very dilute solutions in such solvents as alcohols, ketones, carboxylic acids, or ethers.

The dependence of the position of acid-base equilibria on the dielectric constant of the solvent differs for equilibria of different types.

For instance, when electroneutral or negatively charged acids react with a solvent (S) ions of unlike signs result:

$$A + S \rightleftarrows B^- + SH^+ \quad (a)$$

$$A^- + S \rightleftarrows B^{-2} + SH^+ \quad (b)$$

$$A^{-2} + S \rightleftarrows B^{-3} + SH^+ \quad (c)$$

An increase in the dielectric constant of the solvent should weaken the interionic interaction and shift equilibria of these types (a, b, c) to the right.

No such shift should occur in the case of equilibrium (d):

$$A^+ + S \rightleftarrows B + SH^+ \quad (d)$$

Finally, in the case of equilibria (e) and (f) the opposite effect will be observed because ionization of acids $A^{++}$ and $A^{+++}$ results in the formation of charged ions carrying the same sign.

$$A^{+2} + S \rightleftarrows B^+ + SH^+ \quad (e)$$

$$A^{+3} + S \rightleftarrows B^{+2} + SH^+ \quad (f)$$

Thus, the most important properties of the solvent, influencing the establishment of acid-base equilibrium in solution, are its proton affinity and dielectric constant.

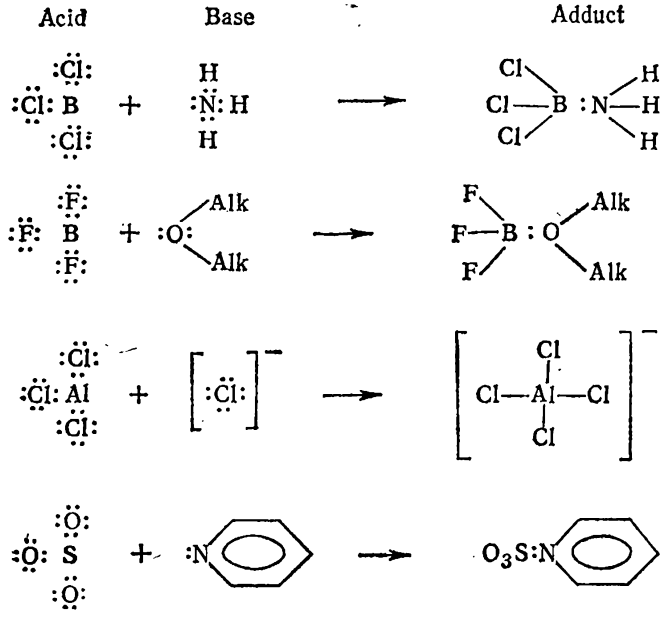
**Theory of Generalized Acids and Bases (Lewis's Theory).** A more general treatment of the acid-base properties of chemical compounds, than that of Brönsted's theory, was proposed by Lewis in 1923 [73, 74]. The Lewis theory has found wide application, especially in describing reactions in non-hydroxylic solvents.

What is the essence of Lewis's theory? As it was shown above, the proton is an acid because it can form a covalent bond with a base through the free (unshared) electron pair of the latter:

$$H^+ + :B \longrightarrow [H:B]^+$$

However there are many electron-acceptor ions and molecules besides the proton, capable of combining with bases through the electron pairs of the latter.

*According to Lewis, all molecules and ions of this type, which are acceptors of electron pairs, are called acids.* Apparently, Lewis applied the "acid" concept not only to protic but to aprotic substances as well; thus the concept of acid becomes broader and more general. The acid-base reaction (neutralization) according to Lewis, consists in the transfer of an electron pair from the base to the acid ("for common use").

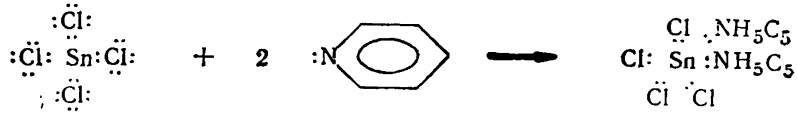


Lewis acids may be of several types. They are, for instance, substances containing atoms with unfilled electron octets.

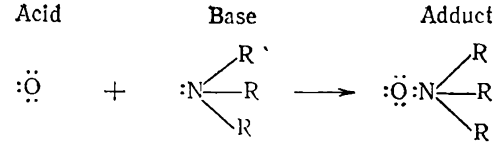
The boron atoms in the molecules of boron trichloride and boron trifluoride, and the aluminium atom in the aluminium trichloride molecule have six valence electrons instead of the maximum of eight. The sulphur atom of sulphur trioxide is also poor in electrons.

Since *Lewis acids* add to the molecules of bases at the place of highest electron density of the latter, they are called *electrophilic reagents.* Similarly, *Lewis bases*, which always attack other molecules at the place where their constituent atomic nuclei are the least screened by electrons, are called *nucleophilic reagents.*

Lewis acids also include molecules such as $SnCl_4$ in which all the atoms are surrounded by an electron octet, but the octet of one of the atoms expands when they react with a base, say, pyridine:



Atoms may be Lewis acids: for example, the oxygen atom in the reaction with tertiary amines, resulting in the formation of amine oxides:




Some cations which are Lewis acids are $H^+$, $Li^+$ and $Ag^+$

| *Acid* | *Base* | *Adduct* |
|---|---|---|
| $H^+$ + | $:NH_3$ | $[H_4N]^+$ |
| $Li^+$ + | $CH_3OH$ | $[CH_3OHLi]^+$ |
| $Ag^+$ + | $:NH_3$ | $[H_3NAg]^+$ |

Of particular importance for organic chemistry is a group of cations, which plays an important part in reactions of aromatic electrophilic substitution, viz.: the nitronium ion $NO_2^+$; the halogen cations, $:\ddot{\underset{\cdot\cdot}{Cl}}^{(+)}$, $:\ddot{\underset{\cdot\cdot}{Br}}^{(+)}$, various acylium ions $R-\overset{+}{C}=O$.

Many reactions of addition at the multiple bonds C = O, C = N, N = O may be considered acid-base reactions in the light of Lewis's theory; for example, the formation of cyanohydrins, chloralhydrate or the alkaline hydrolysis of nitriles:

| *Base* | *Acid* | *Adduct* |
|---|---|---|
| $N\equiv C:^{(-)}$ | $+\ \begin{matrix}R\\ \diagdown\\ C=O\\ \diagup\\ R'\end{matrix}$ | $\rightarrow\ \left[\begin{matrix}R & C\equiv N\\ \diagdown & \diagup\\ & C\\ \diagup & \diagdown\\ R' & O:\end{matrix}\right]^-$ |
| $\begin{matrix}H\\ \diagdown\\ :O:\\ \diagup\\ H\end{matrix}$ | $+\ Cl_3C-\overset{\overset{O}{\|}}{C}-H$ | $\rightarrow\ Cl_3C-\overset{\overset{OH}{\|}}{C}-OH$ <br> $\quad\quad\quad

majority of cases the same molecules and ions may be classified as both Lewis and Brönsted bases:

(a) molecules containing atoms of the fifth, sixth or seventh group of the periodic system with unshared electron pairs (amines, alcohols, ethers, mercaptans, etc.);

(b) anions (e.g., halogen anions, hydroxyl, alkoxyls, carbanions);

(c) alkenes and aromatic hydrocarbons.

**π-Complexes.** Basicity of alkenes and aromatic hydrocarbons in the Lewis sense plays a more important part, than basicity in the Brönsted sense (addition of protons).

A large number of addition products of metallic salts to alkenes and aromatic hydrocarbons are known. By way of example we may mention the adduct of isoamylene and zinc chloride, $(CH_3)_2C = CHCH_3 \cdot ZnCl_2$ [75], ethylene and platinum dichloride, $C_2H_4 \cdot PtCl_2$ [76], stilbene and ferric chloride, $Ph - CH = CH - Ph \cdot 2FeCl_3$ [77], benzene and silver perchlorate, $C_6H_6 \cdot AgClO_4$ [78].

In these complexes the metallic cation is apparently linked with the unsaturated carbon in a definite manner through the π electrons of the hydrocarbon molecule.

In the compounds of benzene with silver perchlorate the silver ion is linked not with a single carbon atom, but, evidently, equally with two neighbouring carbon atoms of the benzene ring through two π electrons. Such adducts are called *π-complexes.*

In the majority of cases it has not been established, whether the adducts of alkenes and aromatic hydrocarbons with Lewis acids are of the π-complex type or whether they are acids linked by an ordinary covalent bond with a definite carbon atom (σ-complex).

When the adduct of a metallic cation (other than proton) can be isolated, the question of its structure could be solved in principle by X-ray diffraction. However, unfortunately, the majority of most important complexes of this sort form in relatively low concentrations in solutions (e.g., during certain substitution reactions in the aromatic series).

Therefore, so far we can only guess about their structures.

Because of this, two different complexes of aromatic hydrocarbons, for instance, of benzene, with hydrogen chloride should be mentioned, one of them (I) forming in the absence, and the other (II) in the presence of aluminium chloride [79].

The first of them is dissociated to a considerable extent even at —79°:

$$C_6H_6 \cdot HCl \rightleftarrows C_6H_6 + HCl$$

It is colourless and does not conduct electric current.

If complex (I) is prepared using deuterium chloride and then reconverted into benzene, the resulting benzene nucleus contains

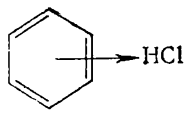
no deuterium:

$$C_6H_6+DCl \longrightarrow \underset{I}{C_6H_6\cdot DCl} \longrightarrow C_6H_6+DCl$$

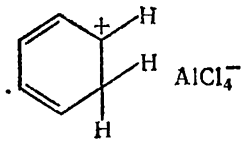
Complex (II) obtained in the presence of $AlCl_3$ is coloured and conducts electric current. If complex (II) is prepared using DCl and the benzene is regenerated, the benzene ring will contain deuterium.

$$C_6H_6+DCl+AlCl_3 \longrightarrow \underset{II}{C_6H_6\cdot DCl\cdot AlCl_3} \longrightarrow C_6H_5D+HCl+AlCl_3$$

It is quite possible that complex I is a $\pi$-complex, while complex II is a $\sigma$-complex.




I




II

**Acid and Base Catalysis.** In organic chemistry reactions catalyzed by acids and alkalies are of great importance. Some of these reactions are catalyzed by both acids and alkalies. Reactions of this type include esterifications, ester, acid anhydride, amide, nitrile, alkyl halide and acyl halide hydrolyses, numerous reactions of addition to the carbonyl group, Claisen, Perkin and Michael condensations, aldol condensations, polymerizations of unsaturated compounds and many others.

Many reactions are accelerated by protic (HF, $H_2SO_4$, $H_3PO_4$) and aprotic acids ($BF_3$, $AlCl_3$, $SnCl_4$).

An analogy may be drawn between the action of acids and bases upon amphoteric solvents and the action of catalysts in reactions [62, 80].

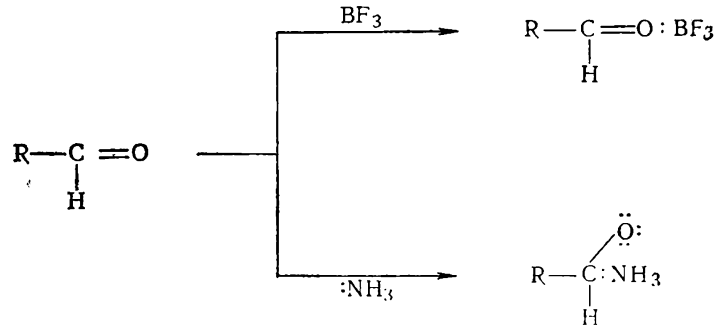
In the same way as the reaction of an acid with a solvent increases the concentration of cations of the solvent and the reaction of a base with the solvent increases the concentration of the anions of the solvent, the addition of an acid catalyst to the reacting substance raises the concentration of acid groups, and the addition of a base catalyst raises the concentration of basic groups participating in the reaction.

For example, aluminium chloride, tin tetrachloride, boron trifluoride and sulphuric acid have the same effect on the reaction of alkylation of aromatic hydrocarbons by alkyl halides, alcohols, ethers and esters; the role of the catalyst consists in the removal

of an anion, resulting in the formation of a reactive alkyl cation:

$$Alk{-}X + A \longrightarrow Alk^+ + AX^-$$
$$Alk^+ + ArH \longrightarrow Ar{-}Alk + H^+$$

Substances, reactions of which are catalyzed by acids and bases exhibit amphoteric properties, for example:




**Strength of Acids and Bases. Electrophilic and Nucleophilic Strength of Reagents.** Acids and bases cannot be arranged in a single sequence on the basis of their relative strength, because the latter depends not only on the solvent, but also on what particular acid (or what particular base) is taken as the basis of comparison. This was first noted by Lewis.

Even in the case of a more limited group of acids—protic acids—their catalyzing capacity in relation to different reactions is not a simple monotonous function of their acid strength, in spite of the fact that here the strength of acids and bases has a simple physical meaning: the strength of an acid depends essentially on the stability of the bond of the hydrogen in the acid molecule, and the strength of a base on its affinity to proton. Lewis acids are quite diversified in character, therefore, naturally, they cannot be arranged in a single series which would hold for all acid-base reactions.

Thus, if we compare the base strengths of $CN^-$, $SO_3^=$ and $NH_3$ in reactions with proton and with the silver cation we get different sequences. For reactions with $H^+$:

$$\underset{(2.5\times10^9)}{CN^-} \geqslant \underset{(1.8\times10^9)}{NH_3} > \underset{(1\times10^7)}{SO_3^=}$$

For reactions with $Ag^+$:

$$\underset{(2.6\times10^{18})}{CN^-} > \underset{(1.7\times10^7)}{SO_3^=} > \underset{(3.3\times10^8)}{NH_3}$$

The numbers in parentheses are the equilibrium constants $K$ of neutralization reactions*.

From this discussion it follows that neither electrophilic nor nucleophilic reagents can be arranged according to their strength in a single series which would hold for all reactions (see page 186).

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*The equilibrium constant of a neutralization reaction is the ratio of concentration of the reaction product of the acid and the base to the product of the concentrations of acid and base:

$$K = \frac{\text{reaction product of acid and base}}{[\text{acid}] \times [\text{base}]}$$

The stronger the base, the higher the equilibrium constant.

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# 2

# SUBSTITUTION AT THE SATURATED CARBON ATOM

## 2-1 TRANSITION STATE CONCEPT

In the general case the course of a chemical reaction depends on two factors: the change in the free energy of the system and the rate of conversion. The first factor is thermodynamic, the second kinetic.

For reactions which are practically irreversible the rate of conversion is the decisive factor, and, therefore, often as a result of a greater rate of conversion the reaction proceeds in a thermodynamically less advantageous direction.

But if the reaction is a reversible one and proceeds at a faster rate, its course is determined by the thermodynamic factor, because the position of equilibrium does not depend on the speed with which it is reached, but only on the ratio of rate constants of the forward and reverse processes.

In the case of reversible reactions which proceed slowly both factors play a part. Organic reactions only in rare instances reach a state of equilibrium, and because of this the results of complex processes are more often determined by the kinetic than by the thermodynamic factor. However, in the general case both factors have a perceptible effect, which makes the study and interpretation of chemical reactions more difficult.

According to the basic approximate equation of the rate of chemical reactions:

$$K = PZ \times e^{-E/RT}$$

the rate constant $K$ is a function of the temperature $T$, the number of collisions between the reacting molecules $Z$, the probability factor $P$ and of the energy of activation $E$ ($R$ is the gas constant, $e$ is the base of natural logarithms).

Thermochemical investigations show that the energy of activation of the reactions of organic compounds is in most cases smaller than the energy of dissociation of these compounds into ions*.

* The same is observed for reactions of covalently bonded inorganic compounds. For example, the energy of dissociation of HI into atoms is 70 kcal/mole (the energy of dissociation into ions is still greater), while the energy of activation of the reaction $2HI \xrightarrow{\text{thermal}} H_2 + I_2$ (in the gas phase) is only 44 kcal/mole.

Thus, organic reactions generally do not proceed through the stage of formation of free ions but through other paths. An insight into these paths is given by the *transition state* or *active complex theory.*

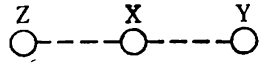
To understand the meaning of the theory of transition states consider the bimolecular substitution reaction:

$$Z + XY \longrightarrow ZX + Y$$

In the reaction between a molecule of reagent Z and a molecule of XY different collisions of these two particles are possible. However, a chemical reaction takes place only when Z approaches the molecule XY along its axis (or at a slight angle from this axis) on the side of the X atom.

(I)

At a definite instant of approach of these two particles a weak bond forms between Z and X with a simultaneous weakening of the X — Y bond:



(II)

At this stage X is already bound with Z to some extent though its bond with Y is not yet broken. Such a state is called a *state of transition* or an *active complex.* As the achievement of such a state

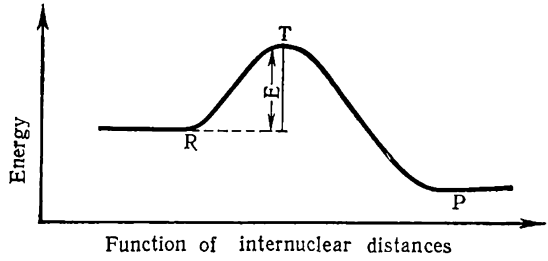
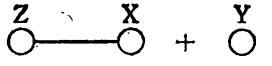



FIGURE 2-1 Energy state of a reacting system

in the approach of the particles Z and XY requires expenditure of energy, in particular, for stretching the X — Y bond, the transition state corresponds to a maximum on the energy curve showing the energy state of the reacting system (Fig. 2-1).

On further approach of Z and X a covalent bond is formed between them and the bond between X and Y is completely broken:



(III)

This process is accompanied by a drop in the energy of the reacting system. Point $R$ (Fig. 2-1) corresponds to the energy of the system, when Z and XY are removed from each other (I), point $P$, of the analogous system ZX and Y (III), point $T$ corresponds to the energy of the state of transition (II). The difference between the energy of the transition state ($T$) and the energy of the initial system

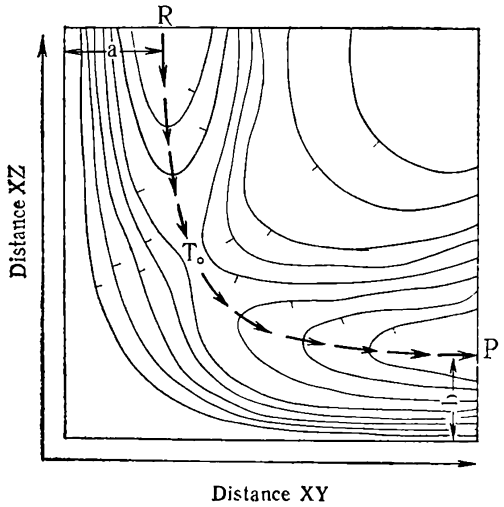



FIGURE 2-2 Change in the energy state of a reacting system (contour map)

($R$) is the activation energy $E$ of the reaction. Thus, the *energy of activation is the energy needed to bring two (or more) reacting particles to a state of active complex.*

The bimolecular substitution reaction $Z + XY \rightarrow ZX + Y$ just considered is conveniently illustrated with the aid of a "contour map" (Fig. 2-2). If the distances between X and Y are plotted as abscissas, and those between Z and X as ordinates and the energy of the system is plotted on an axis perpendicular to the plane of the abscissa and ordinate axes, the change in energy of the system as the reaction proceeds may be expressed by a space curve $RTP$. The broken lines represent "energy contours", each corresponding to a definite constant energy value*. These values increase along the third axis from the minima $R$ and $P$. $R$ lies on the bottom of a "valley" flanked on both sides by "energy hills" and rising to the "energy pass" at $T$, after which a similar "valley" drops to $P$. If Z is at a practically infinite distance from XY, the equilibrium internuclear distance of molecule XY is represented by the distance $a$, and the

* The "contour map" is similar in structure to the representation of relief on geographical maps.

energy of the system (Z + XY) is a minimum. As Z approaches (i.e., ZX decreases) the distance XY increases at first slowly and then more rapidly, as is shown on the curve *RT*. At the same time the energy of the system increases and the system "ascends the valley" to the "pass" at *T* which represents the state of transition. Then X reacts with Z and with Y in equal measure. Upon further approach of Z to X, XY increases and the system "descends the valley" *TP* to *P*. The point *P* corresponds to the system of particles Y and ZX not reacting with each other. The equilibrium internuclear distance of the molecule XZ is represented by the distance *b*, and the energy of the system (ZX + Y) is a minimum at *P*.

The "pass" at *T* represents the energy barrier between XY and XZ; its height is a measure of the energy of the activation process.

$$Z + XY \longrightarrow ZX + Y$$

The less simple process of substitution in a system with four "centres" (of the type YZ + RX → RZ + YX) may be interpreted similarly.

It should be noted that the state of transition corresponds to the maximum on the energy curve and therefore such a system cannot be regarded as an intermediate compound. Any intermediate chemical compound, no matter how low its stability, corresponds to a relative energy minimum, from which the final state can be reached only by again overcoming a certain energy barrier (second maximum—second transition state). Intermediate compounds are real chemical compounds, but the transition state is not a chemical compound in the ordinary sense of the word, and therefore concepts related to real chemical compounds, such as valence, constancy of atomic distances and angles of valence do not apply.

Except for a number of special cases (see page 501), the most important value in organic reactions is the energy of activation *E*. *E* is contained in the exponent of the basic kinetic equation and is therefore the chief factor determining the reaction rate—a comparatively small change in *E* changes the reaction rate by a large factor.

It should, however, be pointed out that the transition state theory does not make it possible at present to calculate activation energies exactly enough to account for the fact that certain organic reactions will proceed predominantly over others. The only way of judging about the factors determining the energy of activation, for instance, of competing organic reactions is by comparing the structures of the active complexes of the competing reactions in a purely qualitative manner and by comparative evaluation of their energies (see pages 492-493). The criterion for deciding whether opinions so derived are correct is naturally experimental data.

## 2-2 CLASSIFICATION OF SUBSTITUTION REACTIONS

The expression "substitution" is generally used to designate reactions in which hydrogen is substituted by another atom or group of atoms. However, in the broader sense of the word substitution (or exchange) reactions may be defined as reactions in which any atom or group of atoms is replaced by another atom or group of atoms according to the general scheme:

$$Z + RX \rightarrow RZ + X$$

or

$$YZ + RX \rightarrow RZ + XY$$

Depending on how the R—X bond is severed, this being determined by the chemical structure of the initial compound and by the nature of the acting reagent, the substitution may be nucleophilic ($S_N$), homolytic ($S_R$) or electrophilic ($S_E$).

Nucleophilic substitution

$$\left.\begin{array}{l} \text{(a)}\ Z^- + R\,\vdots\!-X \longrightarrow R-Z + X^- \\ \text{or} \\ \text{(b)}^*\ Y\,\vdots\!-Z + R\,\vdots\!-X \longrightarrow R-Z + Y-X \end{array}\right\} S_N$$

Homolytic substitution

$$\left.\begin{array}{l} \text{(a)}\ Z\cdot + R\,\vdots\!\cdot X \longrightarrow R-Z + \cdot X \\ \text{or} \\ \text{(b)}\ Y\,\vdots\!\cdot Z + R\,\vdots\!\cdot X \longrightarrow R-Z + Y-X \end{array}\right\} S_R$$

Electrophilic substitution

$$\left.\begin{array}{l} \text{(a)}\ Z^+ + R-\vdots X \longrightarrow R-Z + X^+ \\ \text{or} \\ \text{(b)}\ Y-Z + R-\vdots X \longrightarrow R-Z + Y-X \end{array}\right\} S_E$$

### 2-2.1 Nucleophilic Substitution

**Two Mechanisms of Nucleophilic Substitution ($S_N1$ and $S_N2$).** Numerous investigations of nucleophilic substitution reactions in the alkane series, especially hydrolysis and alcoholysis of alkyl halides carried out largely by Ingold, Hughes and collaborators

* It is self-evident that reaction (b) represents nucleophilic substitution of Z for X at the saturated carbon atom of an organic group R. The same reaction also represents electrophilic substitution of R for Y in the Y—Z molecule (or Y for R in the R—X molecule). The same applies to reaction (b) of the electrophilic substitution. The relations indicated are similar to those observed in the case of the oxidation-reduction reactions.

ed chemists to the belief that there are two mutually exclusive nechanisms of nucleophilic substitution.

In the simplest case, if there are three centres in the molecules of the substance and if during the reaction only one bond is broken, hen the nucleophilic substitution reaction may be represented by wo schemes:

$$Z + R{-}X \longrightarrow R{-}Z + X \Big\} S_N2 \quad \text{(bimolecular nucleophilic substitution)}$$

$$\left.\begin{array}{l} R{-}X \xrightarrow{\text{Slow}} R^+ + X^- \\ R^+ + Z^- \xrightarrow{\text{Fast}} R{-}Z \end{array}\right\} S_N1 \quad \text{(monomolecular nucleophilic substitution)}$$

The first mechanism ($S_N2$) of nucleophilic substitution is perfectly clear. This is the mechanism of an ordinary bimolecular substitution reaction, the current interpretation of which is described on pages 103-104. This process proceeds through a transition state and consists of the addition of one group (Z) and simultaneous elimination of another (X). This reaction is single-stage and obviously bimolecular.

The second mechanism ($S_N1$) is that of a two-stage reaction. The first (slow) stage consists in dissociation of the molecules into ions; in the second stage the ions formed react quickly, yielding the end product. Thus, in $S_N1$ the elimination of one group (X) and the addition of another (Z) does not take place simultaneously, but slow elimination of X is followed by rapid addition of Z. Because the slowest stage of this reaction is monomolecular, the entire reaction is monomolecular.*

The $S_N1$ mechanism is impossible when the group X is linked very strongly to a hydrocarbon group, say, to an aromatic nucleus. Because of this the assumption of two mechanisms for nucleophilic substitution applies mainly to substitution reactions in the aliphatic series.

Proofs of the existence of two different mechanisms of nucleophilic substitution may be obtained by examining, for instance, whether the experimental data available on the hydrolysis and alcoholysis of alkyl halides agree with the hypothesis of the existence of two mechanisms ($S_N2$ and $S_N1$) for these processes.

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* The ionization, that occurs when the reaction proceeds according to mechanism $S_N1$, is regarded as solvolytic ionization. This means that "monomolecular" ionization is actually "polymolecular", because solvent molecules (for instance, water) participate in the reaction. However, from this standpoint all the reactions taking place in solution should be considered polymolecular.

To avoid this it has been suggested to consider a reaction monomolecular if only one type of molecules undergo "covalent changes", and bimolecular if two types undergo these changes.

For the hydrolysis of alkyl halides the two mechanisms may be represented as follows:

$$\left.\begin{array}{l} OH^- + R-X \longrightarrow R-OH + X^- \text{ or} \\ H-OH + R-X \longrightarrow R-OH + X^- + H^+ \end{array}\right\} S_N2$$

$$\left.\begin{array}{l} R-X \xrightarrow{\text{Slow}} R^+ + X^- \\ R^+ + OH^- \xrightarrow{\text{Fast}} R-OH \text{ or} \\ R^+ + H-OH \xrightarrow{\text{Fast}} R-OH + H^+ \end{array}\right\} S_N1$$

It is natural to assume that occurrence of the reaction predominantly according to the one or the other mechanism must depend on the nature of R and X in RX, on the nature of the reagent Z, and on the reaction conditions.

Theoretically one should expect that successive changes in the electron-donor properties of the R groups will exert a different influence on the $S_N2$ and $S_N1$ reactions. Thus, with increasing electron-donor (electronegative) properties of R, attack of the molecule in the $S_N2$ mechanism by the reagent RX, having a free electron pair, be it $OH^-$ or H — O — H, should become more and more difficult; on the other hand, ionization, which determines the rate of reaction proceeding according to mechanism $S_N1$, will become easier.

If R is changed in the direction indicated over a sufficiently large range, the reactions should first proceed according to mechanism $S_N2$ at slower and slower rates, and then switch over to mechanism $S_N1$ at increasing rates [1].

Experimental data on the hydrolysis of a series of alkyl halides RX with groups, possessing increasing electron-donor properties [R = $CH_3$, $C_2H_5$, $CH(CH_3)_2$, $C(CH_3)_2$], corresponds fully to the above assumptions.

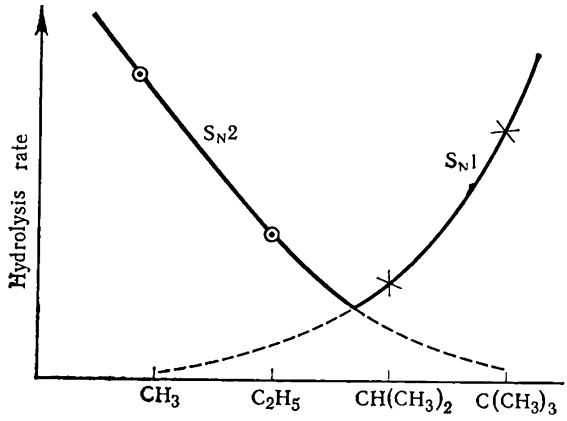
Hydrolysis of $CH_3X$ and $C_2H_5X$ with alkali in alcohol or aqueous alcohol is a bimolecular reaction; $C_2H_5X$ reacts slower than $CH_3X$.

Kinetic measurements of the hydrolysis of $(CH_3)_2CHX$ in aqueous alcohol showed that the hydrolysis takes place simultaneously according to both bimolecular and monomolecular mechanisms, the rate of the bimolecular reaction being slower than the rate of hydrolysis of $C_2H_5X$ [2].

Hydrolysis of $(CH_3)_3CX$ in aqueous alcohol or in aqueous acetone takes place monomolecularly; the rate of the reaction is much greater than that for $(CH_3)_2CHX$ under the same conditions [3]. The rate of hydrolysis of $(CH_3)_3CX$ is independent of the presence or absence of alkali. This transition from $S_N2$ to $S_N1$ in the series $CH_3X$, $C_2H_5X$, $(CH_3)_2CHX$, $(CH_3)_3CX$ shows that in the $S_N1$ mechanism

he nucleophilic reagent does not attack the molecule of the initial ubstance and the rate measured is the rate of ionization which is ided by the supply of electrons from R.

The relative rate of hydrolysis of alkyl halides is presented in 'ig. 2-3.




IGURE 2-3 Rate of hydrolysis of alkyl halides as a function of the nature of alkyl radicals [4]

A quantitative comparison of the relative rates of hydrolysis f alkyl bromides is given below [5]:

| | |
|---|---|
| $CH_3Br$ | 2,140 |
| $CH_3CH_2Br$ | 171 |
| $(CH_3)_2CHBr$ | 5 |
| $(CH_3)_3CBr$ | 1,010 |

The values given are the sums of the first- and second-order constants.)

Other primary alkyl groups favour the same reaction mechanism 'hich applies in case of $CH_3$ and $C_2H_5$, because the induction effects f *n*-alkyl groups differ but slightly from one another. Secondary lkyl groups resemble isopropyl, and tertiary ones, *tert*-butyl.

Of interest also is the series of halogen derivatives: $CH_3X$, $_6H_5CH_2X$, $(C_6H_5)_2CHX$, $(C_6H_5)_3CX$.

Whereas $CH_3X$ hydrolyzes according to a bimolecular mechanism, he kinetics of alkaline hydrolysis of benzyl chloride is not so simple 5]. Diphenylchloromethane hydrolyzes in aqueous alcohol accord- ıg to a monomolecular mechanism; in this case hydrolysis is inde- endent of the addition of alkali [7]. Triphenylmethyl chloride onducts electric current when dissolved in ionizing solvents. It is lear that the hydrolysis of benzyl chloride proceeds simultaneously ccording to both monomolecular and bimolecular mechanisms;

this explains why alkaline hydrolysis (which favours $S_N2$ because of the relatively high concentration of OH ions) is accelerated in the presence of electron-acceptor substituents in the nucleus of benzyl chloride, while in the absence of alkali (when conditions are less favourable for $S_N2$) the same substituents decrease the rate of hydrolysis.

When substitution reactions follow the $S_N1$ mechanism, the change in electronegativity of the second reagent (Z) should not affect the rate of reaction, because the latter is determined by the rate of the slowest reaction stage (ionization), in which the second reagent does not participate (page 108).

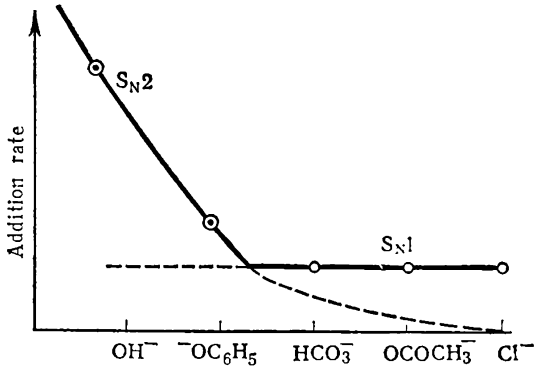



FIGURE 2-4 Rate of substitution of halogens in alkyl halides by ions of different electronegativity

On the other hand, if the substitution takes place according to the $S_N2$ mechanism a change in electronegativity of the second reagent should influence the rate of the process. The low electronegativity of Z should help it to acquire an electron pair for the formation of the covalent bond R — Z, so that the transition state Z...R...X should be attained with a smaller activation energy in this case.

Thus, lowering the electronegativity of Z should promote an increase in the reaction rate of substitution according to $S_N2$.

From the above it follows that if different reagents (Z) are taken in the order of increasing electronegativity, the reactions will take place slower and slower according to the $S_N2$ mechanism, and then will switch to the $S_N1$ mechanism and proceed at a constant rate.

This hypothesis has been confirmed experimentally [8], as is evident from Fig. 2-4, where the capacity of Z to attract electrons increases from left to right.

Proofs of the existence of the two mechanisms of nucleophilic substitution ($S_N2$ and $S_N1$) would be greatly simplified if the order

f a reaction could be considered a reliable criterion of its kinetic nechanism. However, it must be kept in mind that constancy of he rate coefficient of the first order, obtained in the hydrolysis n aqueous alcohol of such alkyl halides as *tert*-butyl chloride is not 'et proof of the monomolecular mechanism of this reaction. In such olution two reactions take place:

$$R{-}Cl + H{-}OH \longrightarrow R{-}OH + HCl$$
$$R{-}Cl + HO{-}C_2H_5 \longrightarrow R{-}OC_2H_5 + HCl$$

As water and alcohol are present in excess, the reaction will nevitably be a first-order one (pseudomonomolecular in the case f a bimolecular reaction)*.

The principal proof that the reaction has a monomolecular mecha- ism is that the rate of reaction is independent of the addition of $OH^-$, since if the reaction follows the $S_N2$ mechanism, the addition o the water of a stronger nucleophilic reagent, such as hydroxyl on, will increase the rate of reaction.

To enable determination of the kinetic mechanism of a reaction rom its order, the concentrations of both reagents must be relative- y low.

These conditions were adhered to when investigating the reaction f $(CH_3)_3CCl$ with a small amount of water in formic acid solution, he high ionizing power of which favours the reaction taking place ccording to a monomolecular mechanism [9]. Under these condi- ions it was demonstrated that the reaction rate does not depend n the concentration of the water, i.e., that the hydrolysis is a mono- iolecular reaction. Conversely, the rate of hydrolysis of *n*-butyl romide under the same conditions increased linearly with increasing 'ater concentration, which confirms the bimolecular character f the latter reaction.

Further investigation of the hydrolysis of alkyl halides with mall amounts of water in formic acid showed that the order of the hange in reaction rates for different groups is as follows:

$$CH_3 < C_2H_5 < CH(CH_3)_2 < C(CH_3)_3$$

This is clearly the order which would be expected from reactions ollowing the mechanism $S_N1$ (the rate of ionization grows with the ncreasing electron-donor properties of the alkyl groups).

From the experiments on the hydrolysis of alkyl halides in formic cid it follows that the predominance of $S_N2$ or $S_N1$ depends also n the medium in which the substitution reaction takes place. 'nder favourable conditions hydrolysis of all the alkyl halides ıay follow the $S_N1$ mechanism.

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* As is the case with the inversion of sucrose $C_{12}H_{22}O_{11} + H_2O \rightarrow 2C_6H_{12}O_6$.

The above-mentioned kinetic proofs of the monomolecular mechanism of hydrolysis refer to the case where both reagents are present in small controllable concentrations. Kinetic proofs of the existence of mechanism $S_N1$ for cases where one of the reagents is a solvent and is therefore present in a large excess have also been obtained [10].

Hydrolysis of alkyl halides according to $S_N1$ may be described by the following equations:

$$R-X \underset{(2)}{\overset{(1)}{\rightleftharpoons}} R^+ + X^- \xrightarrow[(3)]{HOH} R-OH + H^+ + X^-$$

The first (measurable) stage of the reaction is reversible, and if the rate of reaction (2) is significant as compared with that of reaction (3), the accumulation of halide ions as the reaction proceeds makes reaction (2) progressively more and more important, as a result of which the measured rate (representing the rate of increase of the halide ion concentration) should fall off.

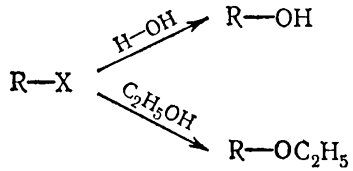
With reactions following a bimolecular mechanism the reaction rate does not slow down; these reactions proceed (in the presence of excess water) at a constant first-order rate.

Moreover, addition of the $X^-$ contained in R — X should lower the rate of a reaction following a monomolecular mechanism, but will have no effect on the rate of a reaction proceeding according to a bimolecular mechanism.

All these theoretical assumptions have been confirmed experimentally [10].

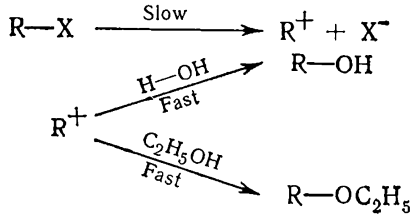
Confirmation of the monomolecular nature of solvolytic reactions of *tert*-butyl halide and certain other halogen derivatives was obtained by comparing reaction rates and ratios of reaction products formed under definite conditions.

If an alkyl halide undergoes hydrolysis and alcoholysis simultaneously in aqueous alcoholic solution according to bimolecular mechanisms:




the reaction products (alcohol and ether) are formed in the course of a single-stage process with an experimentally measurable reaction rate. Because of this the ratio of reaction products can be calculated beforehand on the basis of the experimentally determined reaction rate [11].

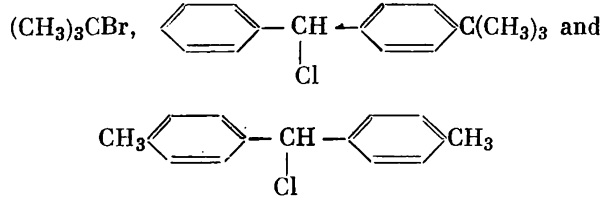
On the other hand, if an alkyl halide undergoes hydrolysis in an aqueous alcoholic solution and simultaneously alcoholysis according to a monomolecular mechanism:




the measurable rate will be the rate of ionization (the slowest step). The subsequent fate of the $R^+$ cation has no effect on the measured rate. Since the reaction products are formed as a result of the second fast step of reaction rather than of the first, slow one, there should be no direct connection between the measured reaction rate and the ratios of the resultants.

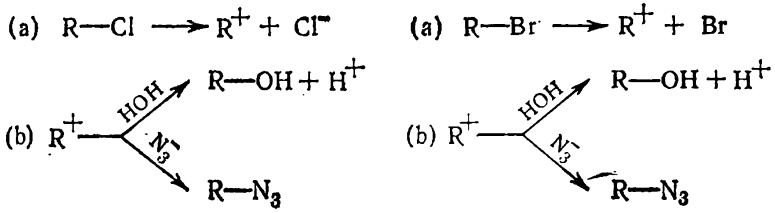
Experiment shows [12] that in the case of *tert*-butyl halides (the solvolytic reactions of which have been proved above in various ways to have monomolecular mechanisms) the ratios of the products formed are not related to the reaction rate, as is to be expected for substances reacting according to the $S_N1$ mechanism.

Analogous experiments on the reactions of alkyl halides with sodium azide in aqueous solution (two reactions take place simultaneously: with water and with the azide ion) also gave the expected results, showing a lack of any correlation between the rate of reaction and the ratios of alcohol and alkyl azide formed for the following halogen derivatives [10].




Finally, if reactions of the type just considered are carried out with alkyl halides having the same alkyl groups but different halide atoms, the same ratio of reaction products should be expected in each case, provided the reactions follow the $S_N1$ mechanism. For example, when reacted with an aqueous solution of sodium azide, alkyl chloride and the corresponding alkyl bromide should give identical mixtures of alcohol and alkyl azide, because these sub-

stances are formed from the same cation in both cases:




In the case of reactions following bimolecular mechanisms there is no reason to expect such identity.

Experimental investigations have shown that the reactions of chloro- and bromodiphenylmethane with aqueous acetone (the mechanism of which was proved to be monomolecular by other means) result in an identical mixture of benzhydrol and benzhydrylazide [10].

All that has been said above leaves no doubt of the existence of two mutually exclusive mechanisms of nucleophilic substitution at the saturated carbon atom.

**Increased Reactivity of Allyl and Benzyl Halides.** It is known that allyl and benzyl halides possess higher reactivity in nucleophilic substitution reactions than alkyl halides. It is interesting that this increased reactivity is manifested both in monomolecular ($S_N1$) and bimolecular ($S_N2$) reactions.

Let us first consider the allylic systems, taking allyl chloride as an example. It undergoes hydrolysis according to an $S_N1$ mechanism (in formic acid media) 25-30 times faster than *n*-propyl chloride.

The hydrolyses of both propyl chloride and allyl chloride in formic acid are two-stage reactions, the slow stage of which, determining the rates of the reactions, is the halide ionization stage (*a* and *a'*):

$$\text{(a)}\ CH_3—CH_2—CH_2—Cl \xrightarrow{\text{Slow}} CH_3—CH_2—CH_2^+ + Cl^-$$

$$\text{(b)}\ CH_3—CH_2—CH_2^+ + H_2O \xrightarrow{\text{Fast}} CH_3—CH_2—CH_2—OH + H^+$$

$$\text{(a')}\ CH_2=CH—CH_2—Cl \xrightarrow{\text{Slow}} CH_2=CH—CH_2^+ + Cl^-$$

$$\text{(b')}\ CH_2=CH—CH_2^+ + H_2O \xrightarrow{\text{Fast}} CH_2=CH—CH_2—OH + H^+$$

The ease with which the slow steps *a* and *a'* proceed, apparently, should depend on the stability of the cation formed (contained in the ionic pair): the stabler the cation the easier it forms. But the stability of the cation will be the higher, the more the positive charge is delocalized, because the presence of a whole positive charge at one carbon (for example in $CH_3^+$) causes high energy (and instability) of the cation. Conversely, distribution of the positive charge

among several carbon atoms (as, for example, in $[(C_6H_5)_3C]^+$) makes the cation stabler (and lowers its reactivity).

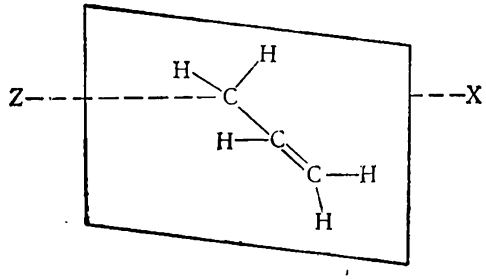
The allyl ion is more stable than the *n*-propyl ion, because its positive charge is not localized at one carbon atom but is distributed equally among the two equivalent carbon atoms of the methylene groups:

$$\overset{\delta+}{C}H_2{=}CH{-}\overset{\delta+}{C}H_2 \quad \text{or} \quad \left[CH_2{\cdots}CH{\cdots}CH_2\right]^+$$

Therefore during ionization of the corresponding halides the allyl cation forms more readily than the propyl cation; the slow stage of $S_N1$ reactions (and consequently the process as a whole) should proceed faster in the case of allylic systems.

The reactivity of allyl halides is also higher in reactions of bimolecular nucleophilic substitution ($S_N2$). The reaction proceeds 20-40 times faster (depending on the second reagent) with allyl chloride than with *n*-propyl chloride.

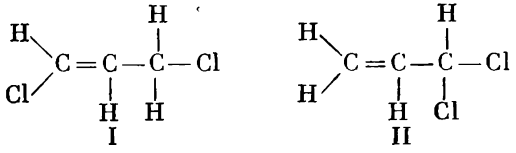
Of great importance here, apparently, is the steric factor. The vinyl group (all five atoms of which are located in one plane) creates less steric hindrance (as compared with the ethyl group) to achievement of the intermediate stage of the $S_N2$ reaction, in which the reaction centre—the carbon atom and the three substituents linked to it—must be arranged in one plane.




On the other hand it is perhaps important for reactions of allylic systems proceeding according to $S_N2$ mechanisms that the intermediate stage can be stabilized by the $\pi$ electrons of the vinyl group overlapping the nascent Z — C and the breaking C — X bonds.

The importance of both the steric and the electronic factor may be illustrated by the reactivity of allyl chlorides chlorosubstituted in positions 1 and 3 in $S_N2$ reactions. The chlorine in position 3 (compound 1) raises its reactivity by drawing the electron density away from the reaction centre, increasing the positive charge of the latter, and thereby facilitating attack by the nucleophilic reagent Z. On the other hand, a chlorine atom in position 3 creates no addi-

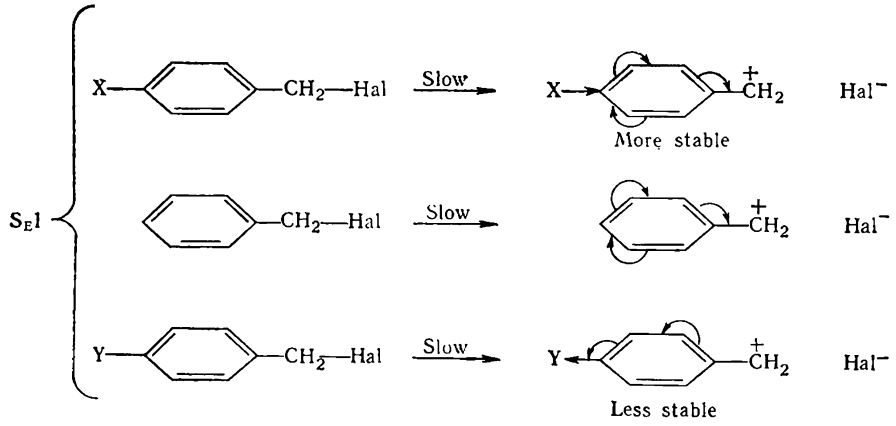
tional steric hindrance to achievement of the intermediate stage, because it is located sufficiently far away from the carbon atom of the reaction centre.



The chlorine in position 1 (compound II) displays an entirely different effect. Though here too the chlorine atom undoubtedly increases the positive charge on the carbon atom, which is the reaction centre, the steric hindrance it creates owing to its proximity to the reaction centre is so great that the rate of the reaction in this case is smaller than for unsubstituted allyl chloride.

The increased reactivity of benzyl halides in $S_N1$ reactions (benzyl chloride, for example, is hydrolyzed in HCOOH 45 times as fast as allyl chloride) and in $S_N2$ reactions (these reactions proceed 200-300 times faster than in the case of alkyl halides) is due to similar causes.

It should be noted, however, that if in the case of $S_N1$ reactions the available data on the rather strong influence of the substituents in the benzene ring (electropositive ones accelerating, and electronegative impeding reactions) are understood, the influence of substituents in $S_N2$ reactions is rather weak, and its nature has not been accounted for satisfactorily in many cases.

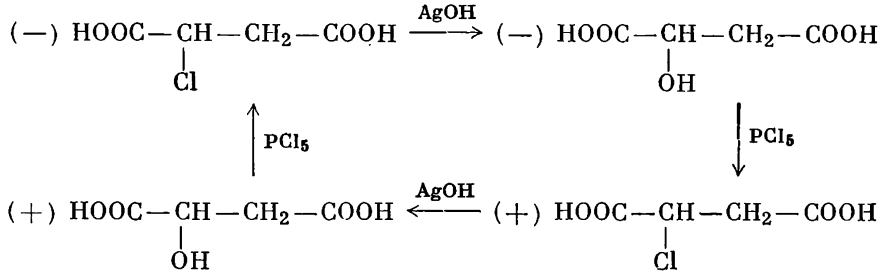



**The Problem of Walden Inversion.** Substitution of a group linked to an asymmetric carbon atom of an optically active compound often results in the formation of a racemic compound. For example, hydrogen bromide reacts with (—) mandelic acid to form inactive bromophenylacetic acid. It is quite evident that in this process of

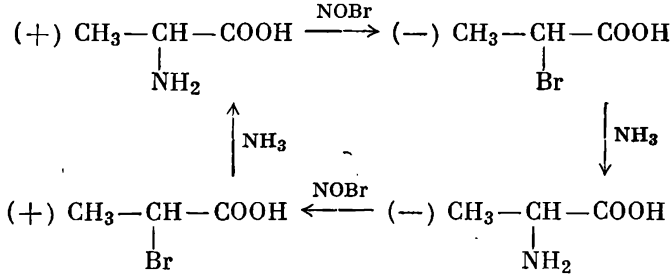
racemization 50% of the compound undergoes inversion of configuration.

In 1896 Walden [13] while investigating halogen substituted succinic acids discovered reactions in which inversion of configuration occurred to a greater extent than 50%, sometimes as high as 100%. This phenomenon, which became known as "Walden inversion", has been studied extensively.

The first example discovered by Walden consisted of the following cycle of transformations:



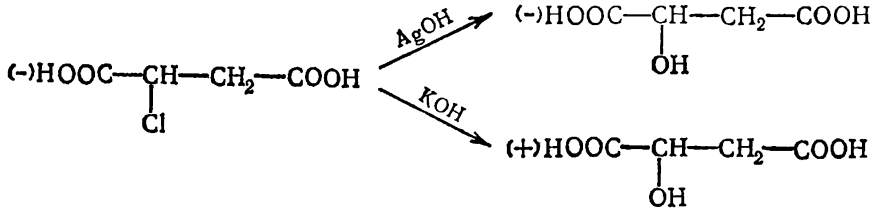

A similar reaction was discovered by Emil Fischer [14]:



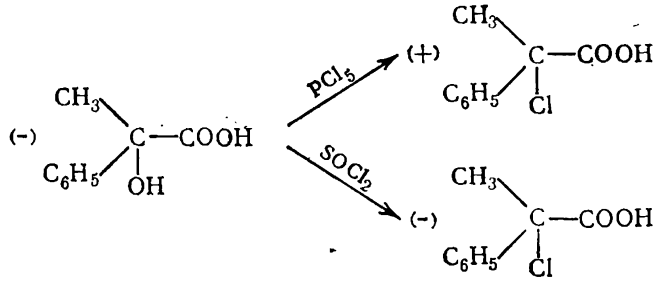

In the transformation of (—) chlorosuccinic acid to (+) chlorosuccinic acid an inversion of configuration must take place in one of the steps (the action of AgOH or $PCl_5$), and when the cycle is completed the inversion must take place twice; the same, naturally, applies also to the second example.

It should not be thought, however, that inversion of configuration occurs in the step which results in a change in the sign of rotation [that is, (—) maleic acid → (+) chlorosuccinic acid], because compounds with similar configurations do not necessarily have the same sign of rotation. Thus lactic acid is levorotatory, but its ethyl ester which has the same configuration is dextrorotatory. Because of this a mere change in the sign of rotation during the reaction is not sufficient evidence of inversion of configuration: the optical antipode of the same compound must be obtained as well.

The same substitution reaction may cause the formation of this or that optical antipode depending on the nature of the second reagent and the conditions of the reaction. This is observed, for example, in the action on (—) chlorosuccinic acid by silver hydroxide on the one hand and by potassium hydroxide on the other [15]:




In some reactions phosphorus pentachloride and thionyl chloride give products with opposite signs of rotation, for example [16]:




It has been shown that the reaction medium also influences the nature of the products formed. For instance, the reaction of ammonia with optically active α-chlorophenylacetic acid may result in an amino acid of one rotation sign or the opposite one depending on the medium [17].

For many years the Walden inversion was considered a puzzling phenomenon which could find no adequate explanation despite the large number of investigations in the field (over 20 theories of the Walden inversion have been suggested).

The fundamental difficulties in the study and explanation of Walden's inversion were the following:

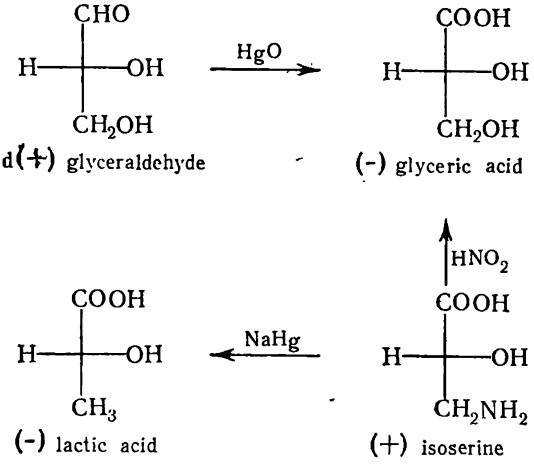
(a) lack of a dependable means of comparing the sign of rotation with the configuration and the consequent difficulty of establishing at what particular step the inversion takes place;

(b) ignorance of the mechanism of substitution at the saturated carbon atom.

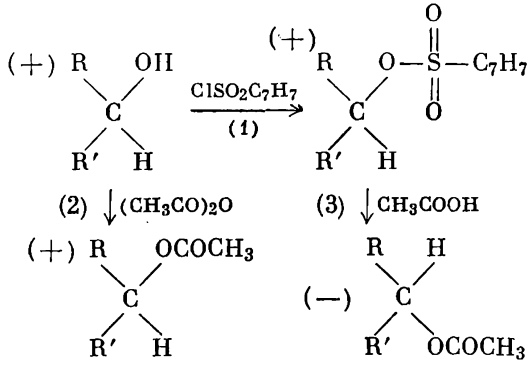
The most considerable advances in establishing the configuration of substances were made by applying the chemical method [18]. To establish the configuration of a substance by this method it is

converted into a substance of a known configuration, using operations which do not involve the asymmetric carbon atom.

For instance, the configuration of levorotatory lactic acid can be established on the basis of the following reactions relating (+)isoserine with *d*(+)glyceraldehyde and (—)lactic acid:




The chemical method makes it possible to establish at what particular stage of a multi-stage chemical reaction the inversion of configuration takes place. This will be illustrated by the following example:




It may be assumed with sufficient confidence that of all the substitution reactions only reaction (3) involves rupture of one of the bonds of the asymmetric atom and therefore this is the only stage where inversion is possible.

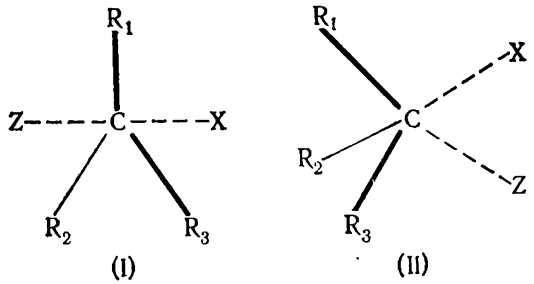
Since the acetate obtained in reaction (2), which does not involve the asymmetric carbon atom, has the same sign of rotation as the alcohol, while the acetate obtained in reaction (3) has the opposite

sign, it may be concluded that the inversion takes place in stage (3) and consequently the alcohol and the acetate having the same sign of rotation possess identical stereochemical configuration. When the substance being investigated cannot be converted into a compound with a known configuration or when it is impossible to do this without involving the asymmetric carbon atom, physical methods may be employed [19].

Thus, at present chemists have sufficiently dependable methods for establishing the stereochemical configurations of substances and for determining in what particular stage of a complex reaction the Walden inversion takes place.

However further study of this phenomenon—its explanation and predictions based on it—would have been impossible, were the mechanism of nucleophilic substitution at the saturated carbon atom not known. Therefore, the greatest advances in explaining Walden's inversion were made by considering this problem in the light of the two mechanisms of substitution reactions in the aliphatic series ($S_N2$ and $S_N1$).

Theoretical consideration shows that bimolecular substitution ($S_N2$) must always be accompanied by inversion of the configuration, because transition state I which causes the inversion should possess much less energy than transition state II, the formation of which would be expected if the configuration were retained (in which case a considerable energy of repulsion of the electrons of the C — X and C — Z "bonds" has to be overcome):




That the bimolecular reaction proceeds through transition state I can be convincingly demonstrated [20] with the aid of radioactive isotopes in the example of the exchange reaction between alkyl halides and halogen ions.

It is known that optically active alkyl halides, the halogen of which is linked with the only asymmetric carbon atom, can be racemized by treatment with a solution of an alkali metal halide with the same halogen. This fact suggests that if racemization is caused by the replacement of the halogen atom in the alkyl halide

by a halide ion, *at least* some of the elementary processes of substitution are inversion.

The use of metal halides with radioactive halides resulted in much more definite conclusions; the rate of substitution was established and it was compared with the rate of loss of optical activity. The following reactions were studied:

$$\overset{*}{I}^- + CH_3-(CH_2)_5-CHI-CH_3 \longrightarrow CH_3-(CH_2)_5-CH\overset{*}{I}-CH_3 + I^-;$$

$$\overset{*}{Br}^- + C_6H_5-CHBr-CH_3 \longrightarrow C_6H_5-CH\overset{*}{Br}-CH_3 + Br^-;$$

$$\overset{*}{Br}^- + HOOC-CHBr-CH_3 \longrightarrow HOOC-CH\overset{*}{Br}-CH_3 + Br^-$$

It was established that all these reactions are kinetically second-order reactions, and hence follow the $S_N2$ mechanism. The rates of these reactions are exactly equal to the rates of loss of optical activity in the initial halogen derivatives. This fact shows that *each* elementary process of bimolecular substitution is accompanied by an inversion of configuration and consequently proceeds through transition state (1).

On the basis of a great deal of experimental data confirming the theoretical assumptions the following general rule was formulated:

*Substitution according to an $S_N2$ mechanism always involves inversion of the stereochemical configuration.* Conversely, full Walden inversion may be regarded as an indicator of bimolecular substitution.

The picture observed in the monomolecular mechanism is much more complex. As the carbonium ion formed during the slow stage of the reaction has planar

$$R_2-\underset{\displaystyle R_3}{\overset{\displaystyle R_1}{\overset{|}{\underset{|}{C}}}}-X \xrightarrow{\text{Slow}} \underset{\displaystyle R_3}{\overset{\displaystyle R_1}{\overset{|}{\underset{|}{C^+}}}}\!\!\!

TABLE 2-1

**Relation Between Optical Activity and the Substitution Mechanism**

| Halogen derivative | Entering group | Reagent | Solvent | Mechanism | Stereochemical result | Optical purity of reaction product in % |
|---|---|---|---|---|---|---|
| $CH_3-(CH_2)_5-CH(CH_3)Cl$ | $OC_2H_5$ | $OC_2H_5^-$ | $C_2H_5OH$ | $S_N2$ | Inverted | ~ 100 |
| $CH_3-(CH_2)_5-CH(CH_3)Br$ | OH | $OH^-$ | 60% aq. $C_2H_5OH$ | $S_N2$ | Inverted | ~ 100 |
| | OH | $H_2O$ | Ditto | $S_N1$ | Racemized + Inverted | 66 |
| | $OC_2H_5$ | $OC_2H_5^-$ | Ditto | $S_N2$ | Inverted | ~ 100 |
| | $OC_2H_5$ | $HOC_2H_5$ | Ditto | $S_N1$ | Racemized + Inverted | 74 |
| | $OC_2H_5$ | $OC_2H_5^-$ | Abs. $C_2H_5OH$ | $S_N2$ | Inverted | ~ 100 |
| $C_6H_5-CH(CH_3)Cl$ | OH | $H_2O$ | $H_2O$ | $S_N1$ | Racemized + Inverted | 17 |
| | OH | Ditto | 60% aq. acetone | $S_N1$ | Racemized + Inverted | 5 |
| | OH | Ditto | 80% aq. acetone | $S_N1$ | Racemized + Inverted | 2 |
| | $OCH_3$ | $OCH_3^-$ | $CH_3OH$ | $S_N2$ | Inverted | High |
| | $OCH_3$ | $HOCH_3$ | $CH_3OH$ | $S_N1$ | Racemized + Inverted | Low |
| | $OC_2H_5$ | $OC_2H_5^-$ | $C_2H_5OH$ | $S_N2$ | Inverted | High |
| | $OC_2H_5$ | $HOC_2H_5$ | $C_2H_5OH$ | $S_N1$ | Racemized + Inverted | Low |

(*Continued*)

| Halogen derivative | Entering group | Reagent | Solvent | Mechanism | Stereochemical result | Optical purity of reaction product in % |
|---|---|---|---|---|---|---|
| $C_6H_5$, $CH_3$, CHBr | OH | $H_2O$ | $H_2O$ | $S_N1$ | Racemized + Inverted | Low |
| $HO_2C$, $CH_3$, CHBr | OH | $H_2O$<br>$H_2SO_4$ | $H_2O$ | $S_N2$ | Inverted | ~ 100 |
| $CH_3O_2C$, $CH_3$, CHBr | $OCH_3$<br>$OCH_3$ | $OCH_3^-$<br>$HOCH_3$ | $CH_3OH$<br>$CH_3OH$ | $S_N2$<br>$S_N2$ | Inverted<br>Inverted | ~ 100<br>~ 100 |
| $-OOC$, $CH_3$, CHBr | OH<br>OH<br>$OCH_3$<br>$OCH_3$ | $OH^-$<br>$H_2O$, $OH^-$<br>$OCH_3^-$<br>$OCH_3^-$, $HOCH_3$ | $H_2O$<br>$H_2O$<br>$CH_3OH$<br>$CH_3OH$ | $S_N2$<br>$S_N1$<br>$S_N2$<br>$S_N1$ | Inverted<br>Retained<br>Inverted<br>Retained | ~ 100<br>~ 100<br>~ 100<br>~ 100 |

degree, preventing the second reagent from attacking the side at which the halide was linked with the alkyl cation. Therefore, the second reagent attacks the alkyl cation predominantly on the side opposite to that with which the halogen atom was linked. In this case the formation of a considerable amount of optically active substance with inverted configuration should be expected besides the racemate. But if the alkyl cation is stable, it exists for a relatively long time, sufficient for removal of the halide anion to a considerable distance. In this case the halide anion will have no substantial "screening effect", so that the racemate formed may be expected to have only a minor admixture of the optically active substance with inverted configuration.

On ionization (first stage of $S_N1$ mechanism) of the two halogen derivatives—2-halooctane and α-haloethylbenzene

$$CH_3-(CH_2)_5-\underset{\displaystyle X}{\underset{|}{CH}}-CH_3 \quad \text{and} \quad C_6H_5-\underset{\displaystyle X}{\underset{|}{CH}}-CH_3^-$$

the latter compound should give a more stable cation*, and therefore, hydrolysis of optically active α-haloethylbenzene should result in a higher percentage of the racemized compound and a smaller percentage of the optically active substance with inverted configuration, than hydrolysis of optically active 2-halooctane.

Actually, on hydrolysis of optically active α-chloroethylbenzene according to the $S_N1$ mechanism 83 to 98% of racemized material and 2 to 17% of optically active inverted material are formed [21] depending on the conditions of the reaction; but hydrolysis of 2-bromooctane according to the $S_N1$ mechanism yields 66% of racemized substance and 34% of inverted substance [22].

The effect of the concentration of the reagent upon the ratio of racemic to inverted compounds will be clear from the following discussion.

If the reagent concentration is small, the alkyl cations may have the time in the majority of cases to assume a planar configuration and depart from the halogens hitherto linked to them; if they are attacked only subsequent to this by the particles of the second reagent (the probability of attack from either side being equal), then a predominantly racemic product forms. If, on the contrary, the concentration of the reagent is high, there is a greater probability that they will be attacked by just formed alkyl cations which are still "screened" by halogen ions. In this case a larger percentage of optically active inverted reaction products is to be expected.

Hydrolysis of α-chloroethylbenzene yielded the following data:

| | *Inversion* % | *Racemization* % |
|---|---|---|
| In aqueous 80% acetone | 2 | 98 |
| In aqueous 60% acetone | 5 | 95 |
| In pure water | 17 | 83 |

Thus, in agreement with theory, raising the concentration of the reagent increases the percentage of the inverted compound and decreases the percentage of the racemized compound.

Table 2-1 compares the experimental results obtained on hydrolysis and alcoholysis of a number of alkyl halides under different conditions.

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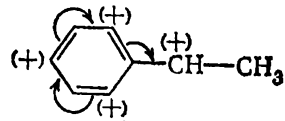
* The cation $C_6H_5-\overset{+}{C}H-CH_3$ is more stable than $CH_3(CH_2)_5-\overset{+}{C}H-CH_3$, because contrary to the latter, it does not possess a whole positive charge, localized on one carbon atom:

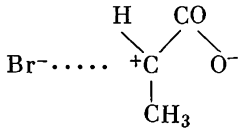



For this reason its energy, and therefore, reactivity, is lower (and its stability higher).

It is rather difficult to account for the retention of configuration (for example, in the hydrolysis and alcoholysis of the bromopropionate ion).

The following hypothesis was suggested to explain the lack of inversion [23].

The first stage of monomolecular substitution results in a betaine-like ion:



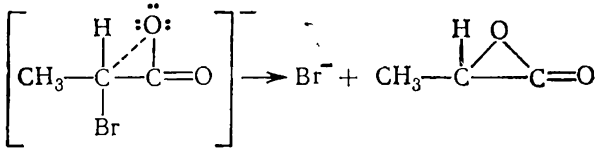
The presence of a charged group of the opposite sign stabilizes the cation, while quantum-mechanical considerations indicate that the pyramidal configuration of the cation is retained.

In the process of ionization the negatively charged carboxyl ion must be oriented directly away from the retreating ion.

Thus, it protects one side of the cation from the entering substituent, and the latter enters the space vacated by the old substituent.

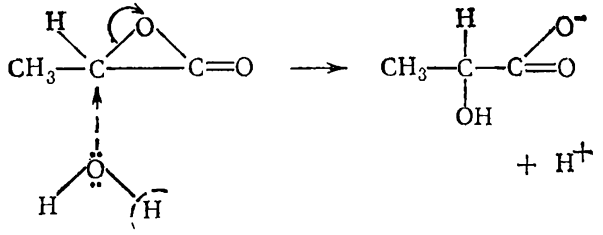
The result must be full or partial retention of configuration depending on whether the betaine-like ion had time to assume its natural configuration fully before the new substituent entered.

Another explanation depends on the assumption that α-lactone forms [24]:

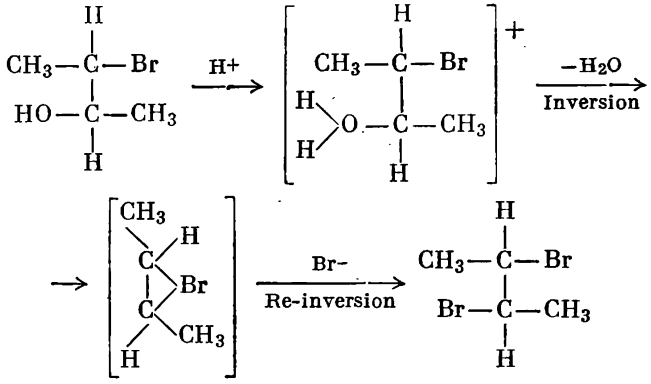


Whether an intranucleophilic substitution takes place or whether the reaction is due to the action of the solvent, the configuration at the α-carbon atom must be inverted.

Retention of configuration may be explained by the very unstable lactone being hydrolyzed rapidly in the second stage. This reaction is also accompanied by inversion:



A similar mechanism [25] (but with the formation of a "bromonium ring") has been suggested from the reaction of 3-bromobutanol-2 with HBr, which takes place with retention of configuration:




This case is more complex because the substitution involves two asymmetric centres.

For reactions proceeding with retention of configuration the unsolved problem is whether the substitution at the asymmetric carbon atom passes through two stages, each of which separately should cause an inversion, or is it a continuous process, wherein the substituent at the neighbouring atom constantly protects the side opposite to that from which the old substituent was eliminated from invasion by the entering substituent.

So far there are no convincing experimental data for the solution of this problem.

For reactions proceeding according to an $S_N1$ mechanism the following general rule may be formulated:

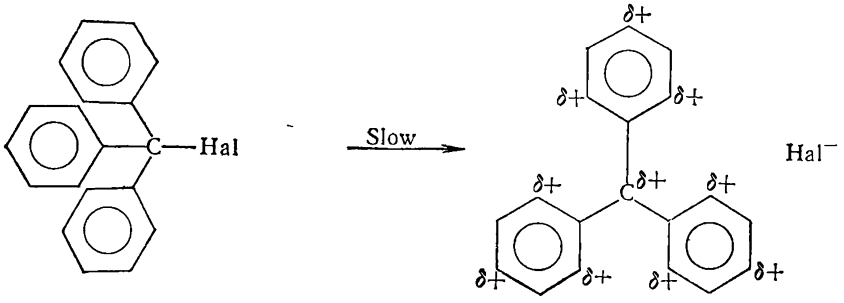
*Substitution according to an $S_N1$ mechanism which passes through a stage of carbonium-ion formation, involves racemization, usually accompanied by inversion of configuration. If the molecule contains a group which fixes the configuration, such as the α-carboxyl ion, configuration is predominantly retained.*

The above discussion shows that the theory of nucleophilic substitution successfully accounts for the Walden inversion; this phenomenon has lost its mystery in many respects and taken up its logical place in the series of other chemical processes. The investigator can now control the Walden inversion by choosing the proper hydrocarbon groups and varying the reagent and the solvent.

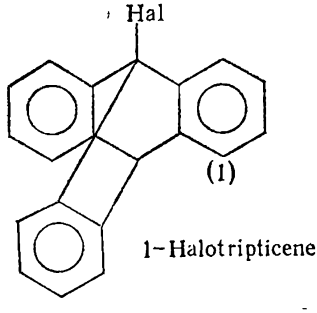
Certain details of this phenomenon are still little understood in the light of the concepts of $S_N1$ and $S_N2$ mechanisms of nucleophilic substitution at the saturated carbon atom. It is hoped that new data on the reaction mechanisms of nucleophilic substitution will help further to clarify and interpret the stereochemistry of these reactions.

**Steric Factors in $S_N$ Reactions.** The inertness of the halogen atom at the "head of a bridge" of rigid systems (such as bicyclic systems) has been known for a long time.

If triphenylmethyl halide readily participates in a reaction of monomolecular nucleophilic substitution as a result of the formation in the course of the slow stage—the ionization reaction—of a stable carbonium ion with a delocalized positive charge, the halogen atom




in the 1-halotripticene molecule (1), where the saturated carbon atom is also linked with one halogen atom and three benzene rings, is inert.




(1)

1-Halotripticene

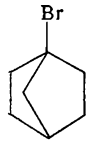
For instance, 1-bromotripticene and 1-iodotripticene do not react with silver nitrate at all. An $S_N2$ reaction is impossible here, because the attack necessary for reactions of this type by the nucleophilic reagent "on the rear" of the C atom, i.e., on the side of it, opposite to where the halogen is located, is excluded because of steric hindrance. Nor is an $S_N1$ reaction feasible because the carbonium ion formed is not planar, and therefore has not only a carbon atom with a localized positive charge, but besides it is sterically strained. All this adds up to the fact that formation of a tripticyl cation would require a large amount of energy.

As we approach the less rigid cyclic systems the probability of $S_N1$ reactions increases, because the intermediate carbonium ions can partly assume a planar configuration.

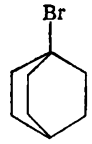
Thus, to substitute hydroxyl for the bromine in 1-bromobicycloheptane (1-bromonorborane) (I) this compound must be heated with an $AgNO_3$ solution at 150° for two days.

For less rigid systems—1-bromobicyclooctane (II) and its dimethyl homologue (III)—four hours' heating is sufficient.

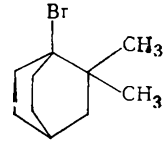
If the solvolysis constant of *tert*-butyl bromide is taken as unity, the solvolysis constants for 1-bromoadamantane (IV), 1-bromobicyclo-(2,2,2)octane (II) and 1-bromonorborane (I) will be $K_1 = 10^{-3}$, $K_1 = 10^{-6}$ and $K_1 = 10^{-14}$, respectively.



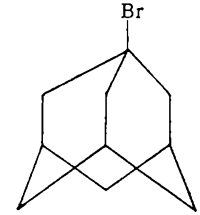
(I)



(II)



(III)



(IV)

As bromoadamantane and bromobicyclooctane are both systems without Bayer's strain, the fact that the reaction rate of the latter compound is 1,000 times slower may evidently be attributed to conformational strain which prevents the formation of carbonium ion in the case of 1-bromobicyclooctane. There is no such conformational strain in the case of 1-bromoadamantane.

**Substitution of Halogen for Hydroxyl.** In all the reactions considered above the halogen atom was replaced by other groups. Results of reactions in which a hydroxyl is replaced by a halogen are given in Table 2-2 [26].

Experimental material for the reactions of alcohols with the phosphorus chlorides and with thionyl chloride (Table 2-2) enables formulation of the following empirical rules regarding the steric results of these reactions.

(1) The action of phosphorus tri- and pentachlorides on alcohols produces compounds with inverted configurations.

(2) The action of thionyl chloride on alcohols is also accompanied by an inversion of configuration, except for cases where a phenyl is linked with the asymmetric carbon atom at which substitution occurs; in this case the reactions involve retention of configuration [27]. This property of α-phenyl substituted alcohols does not show up if the reaction with thionyl chloride is carried out in the presence of pyridine [28].

It is assumed that the first stage of reactions of this type consists in the formation of the esters $ROPCl_2$, $ROPOCl_2$, ROSOCl.

The esters formed may either ionize (eliminating a halogen anion) or undergo $S_Ni$ intramolecular rearrangement*. After ionization of the halide, replacement by the halogen may occur either according to $S_N2$, causing inversion, or according to $S_N1$ which also causes inversion of configuration (when groups fixing the configuration are present, the latter is retained).

In the case of intramolecular rearrangement ($S_Ni$) a heterolytic rupture of the

* The $S_Ni$ mechanism involves a cyclic transitional state (*i* stands for "intra").

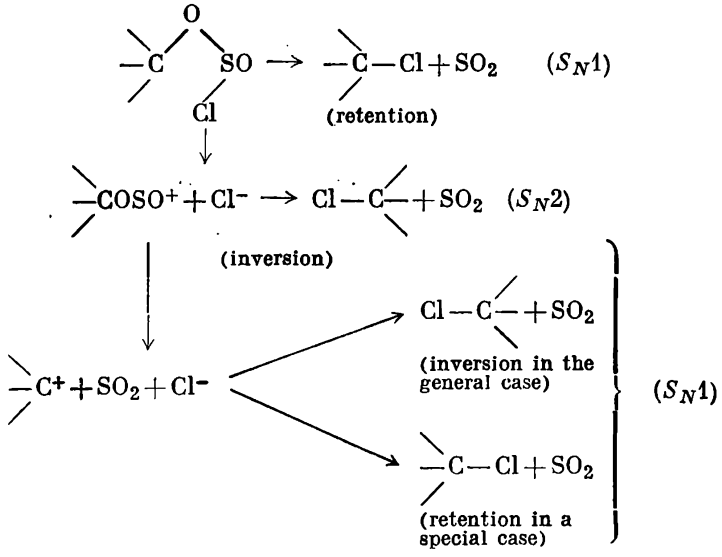
TABLE 2-2
**Steric Effect on the Substitution of Cl for OH***

| | $PCl_3$ | $PCl_3$ + | $POCl_3$ | $POCl_3$ + | $PCl_5$ | $PCl_5$ + | $SOCl_2$ | $SOCl_2$ + | HCl |
|---|---|---|---|---|---|---|---|---|---|
| Octanol-2 . . . . | I | — | I | — | I | I | I | I | I |
| α-Phenylethanol | I | I | I | I | I | I | R | I | I |
| Lactic acid + esters . . . . . | — | — | — | — | I | I | I | I | — |
| Hydroxysuccinic acid + esters | — | — | — | — | I | — | I | — | — |
| Mandelic acid + esters . . . . | — | — | I | I | I | — | R | I | — |
| α-Hydroxy-α-phenylpropionic acid + esters | — | — | — | — | I | — | R | — | — |
| α-Hydroxy-β-phenylpropionic acid + esters | — | — | — | — | I | — | I | — | — |
| β-Hydroxy-β-phenylpropionic acid + esters | I | I | — | — | I | — | R | I | I |

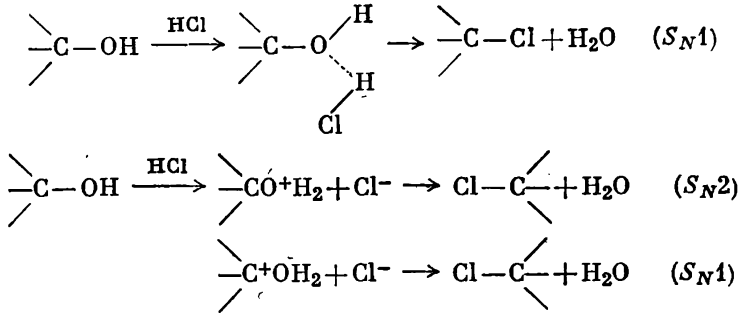
* Only the predominant steric result is given in the table; I — inversion of configuration; R — retention of configuration; dash — reaction not studied.

C—O bond occurs, but without the formation of free ions; the halogen takes the place of oxygen, as a result of which configuration is retained.

The above-described ester transformations are shown in the following diagram for the case of the reaction of alcohols with thionyl chloride:



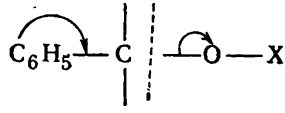
A similar hypothesis was also suggested for the action of hydrogen halides on alcohols:



However, no cases of retention of configuration in the reaction of alcohols with hydrogen halide after an $S_Ni$ mechanism are known as yet.

It was proposed that complexes of alcohols with hydrogen chloride, phosphoric and phosphorous acid chlorides must have a greater tendency to lose their halide ion and a smaller tendency to heterolytic rupture of the C — O bond and intramolecular rearrangement than esters of thionyl chloride.

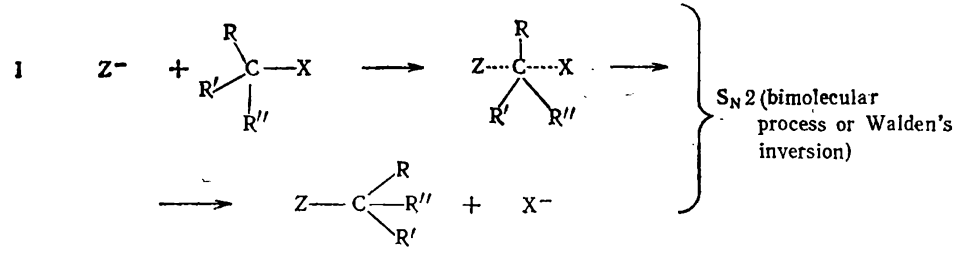
Pyridine and other tertiary amines should facilitate the elimination of the halogen ion because of complex formation (favourable conditions for $S_N1$ and $S_N2$ reactions), and the presence of electron-donor groups, such as phenyl, must facilitate heterolytic rupture of the C — O bond

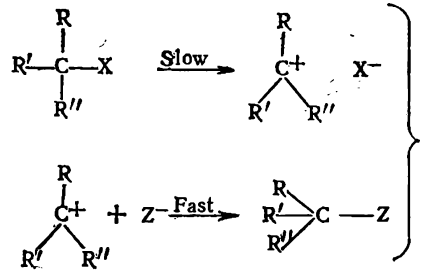


and therefore intramolecular rearrangement ($S_Ni$).

When evaluating the reaction mechanisms of substitution of hydroxyl by halogen, attention should be paid to their greater hypotheticity and poorer experimental basis than is the case with the $S_N1$ and $S_N2$ mechanisms of substitution of halogen in alkyl halides.

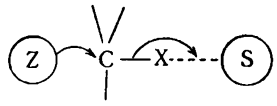
**New Data on the Mechanism of Nucleophilic Substitution.** All the above experimental material on nucleophilic substitution reactions in the aliphatic series is quite well explained by Ingold's theory of $S_N2$ and $S_N1$ mechanisms.



II 


In 1948 a new stage began in the study of the reaction mechanism of nucleophilic substitutions. Swain published a series of papers [29-36] in which he proved that all reactions of nucleophilic substitution have a termolecular mechanism.

According to Swain, in the course of any reaction of nucleophilic substitution the carbon atom must be attacked from the rear by a nucleophilic reagent Z ("push") and the leaving group X must be attacked by an electrophilic reagent, for example, by a solvent molecule S ("pull"):



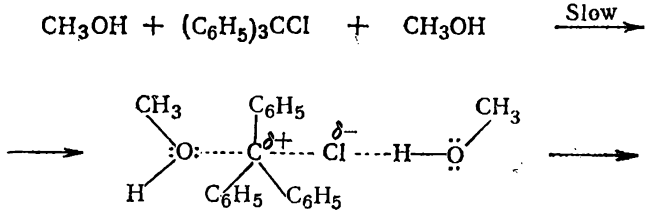
In the English literature this mechanism is called the "push-pull" mechanism".

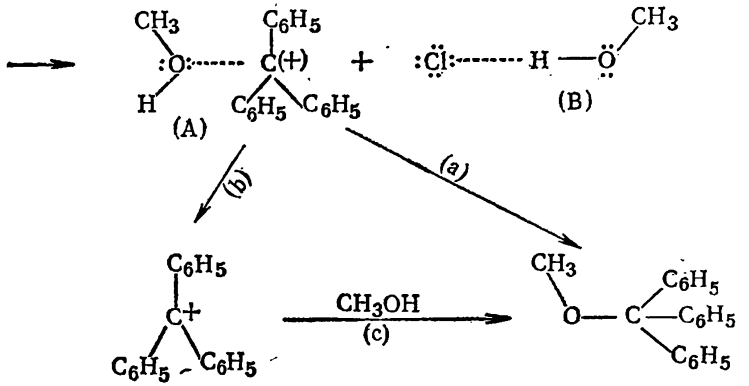
There followed a sharp discussion (still unresolved at present) with Ingold, as a result of which some new features of the mechanism of nucleophilic substitution reactions came to light.

At present it may be concluded from this discussion that Ingold's simple concepts of $S_N1$ mechanism in its original form can no longer explain the new experimental material satisfactorily.

Swain's point of view may be illustrated by the example of the reaction between triphenylmethyl chloride and methanol in benzene [29].

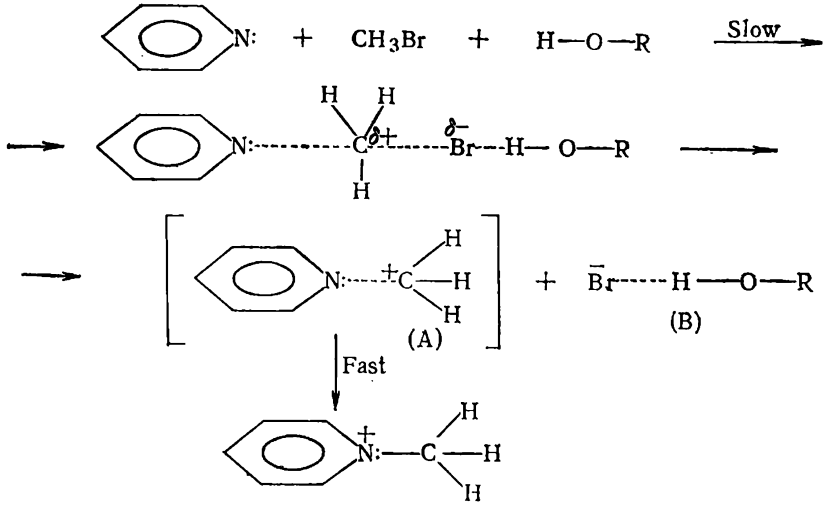
According to Swain this reaction is kinetically third-order (first-order with respect to triphenylmethyl chloride and second-order with respect to methanol). The following mechanism is suggested for the reaction:





The slowest stage of the reaction is a termolecular process; the ion-dipole bond in the solvated cation (A) may change into a covalent one (stage *a*), but it also may break, because of the relative stability of the triphenylmethyl cation (stage *b*). In the latter case the planar triphenylmethyl cation may be attacked by the methanol molecule on either side (stage *c*) with equal probability. Swain calls such a substitution mechanism (as distinct from $S_N1$) "carbonium-ion mechanism".

Nucleophilic substitution reactions in alkyl halides of the methyl halide type differ, according to Swain, from the case just considered only in the nature of the solvated cation (A). Thus, the reaction of methyl bromide with pyridine in the presence of hydroxyl-containing compounds proceeds as follows:



Owing to the low stability of the methyl cation, the carbonium ion (A) does not actually exist in the free state, it is instantaneously converted into a methyl-pyridinium cation.

Swain calls such a substitution mechanism (as distinct from $S_N2$) "mechanism of direct substitution".

Swain also tried to base the idea of termolecular mechanism of nucleophilic substitution reactions at the saturated carbon atom on kinetic investigations

of the reaction of triphenylmethyl chloride with quaternary ammonium salts [33].

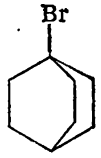
Hawthorn and Cram [37] studied the reaction of triphenylmethyl chloride with substituted benzyl alcohols in benzene solution in the presence of trimethylamine (to neutralize the hydrogen chloride evolved):

$$Ph_3C-Cl + HO-CH_2-C_6H_4X \xrightarrow[(CH_3)_3N]{C_6H_5} PH_3C-O-CH_2-C_6H_4X + HCl$$

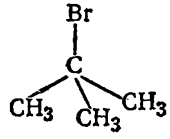
They thought that trimethylamine reacts with triphenylmethyl chloride very slowly, and that this process might therefore be disregarded.

Although Hawthorn and Cram noted a certain discrepancy between the kinetic data obtained by them and Swain's theory of termolecular mechanism, they interpreted their results from Swain's point of view.

Swain's carbonium ion mechanism was questioned by Doering, who studied nucleophilic substitution reactions of 1-bromobicyclooctane (I) in various solvents and found a complete analogy between the behaviour of 1-bromobicyclooctane and *tert*-butyl bromide (II).




I




II

Since in the ionization of 1-bromobicyclooctane solvation of the carbon atom from the side opposite to that where the halogen is located is impossible, the analogous behaviour of substances I and II indicates that this type of solvation is hardly of essential importance for *tert*-butyl bromide either.

Ingold *et al.* published a series of papers [38-43] in 1957, in which they reported the results of a verification of Swain's results.

First of all Ingold showed that the conditions used by Swain for the study of the methanolysis of triphenylmethyl chloride were poorly chosen. This was a source of a number of errors. Swain used pyridine to bind hydrogen chloride, believing that the rate of reaction of pyridine with triphenylmethyl chloride is insignificant. Ingold proved that in reality triphenylmethyl chloride reacts rapidly with tertiary amines and with pyridine in particular. The reaction is reversible, but its rate is 8 times as great as that of methanolysis. Salts of triphenylmethyl chloride $R_3N \cdot (C_6H_5)_3CCl$ react with methanol more slowly than triphenylmethyl chloride.

Study of the methanolysis reaction is complicated by two factors: reversibility and autocatalytic effect, caused by hydrogen chloride. However, the difficulties due to these factors may be avoided to a large extent by measuring the initial reaction rate constants.

Ingold, like Swain, found that the reaction of triphenylmethyl chloride with methanol in benzene was first-order with respect to triphenylmethyl chloride. However, he did not confirm second order with respect to methanol. Actually, the reaction rate constant depends on the concentration of methanol. But this dependence is not subject to a definite relationship. The dependence curve log $K_1 = f \log [CH_3OH]$ has not a constant slope equalling two. The apparent order of the reaction with respect to methanol in the range of reactant concentrations studied varies between 0 and 3 with no definite limitation.

On the basis of these results Ingold came to the conclusion that the reaction has no definite order with respect to methanol.

Similar results were obtained in the reaction between triphenylmethyl chloride and ethanol [44].

If such is the case, one may wonder why the reaction rate constant is dependent on the concentration of methanol.

According to Ingold, methanol not only acts as the nucleophilic reagent, participating independently in the reaction, but also accelerates the reaction, because an increase in the concentration of $CH_3OH$ increases the polarity of the medium. In other words, the rate of the process, according to Ingold, increases due to the addition of polar molecules as a result of electrostatic stabilization of the intermediate state, which is more polar than the initial compounds. Polar molecules influence the intermediate stage from different distances, so that their total action can be described only statistically. Ingold calls this type of kinetic effect "macroscopic co-solvent effect".

As indicated above, Swain discovered phenol to have a strong accelerating effect on the methanolysis of triphenylmethyl chloride in benzene.

Ingold showed that such an accelerating effect is displayed not only by phenol but by other polar substances as well. The effect of polar molecules is not due to their participation in the reaction, because the accelerating effect is exhibited not only by phenol and methanol, which react with triphenylmethyl chloride, but also by such substances as nitromethane and nitrobenzene, which are inert with regard to triphenylmethyl chloride.

Ingold demonstrated further that the reaction has no definite kinetic order with regard to phenol nor with respect to other polar substances accelerating the reaction.

All the experimental results obtained by Ingold in the study of the methanolysis of triphenylmethane in benzene were confirmed in an investigation of the reaction of triphenylmethyl chloride with benzyl alcohols, studied previously by Hawthorn and Cram [37].

Here also it was found that triphenylmethyl chloride reacts much faster with triethylamine than with benzyl alcohol. As the resulting salt, $(C_2H_5)_3N \cdot (C_6H_5)_3CCl$, is less effective in the alcoholysis reaction than triphenylmethyl chloride itself, the addition of a tertiary amine will lower the reaction rate with alcohol in this case too.

Just as in the case of methanolysis the reaction is of first order with respect to triphenylmethyl chloride but has no definite order with respect to the second component, benzyl alcohol. (In the range of concentrations used the order of the reaction with respect to benzyl alcohol varies from 1 to 2.5.)

In the course of the discussion between Ingold and Swain a number of experimental facts were exposed, showing that Ingold's original scheme of the $S_N1$ mechanism is but a first approximation; actually reactions of this type are more complex.

Some of these experimental facts are given below by way of example.

Alcoholysis of triphenylmethyl chloride with methanol proceeds faster than with benzyl alcohol under the same conditions. If both reactions follow an $S_N1$ mechanism (in its simple original form), then equal rates should be expected, because stage (*a*) of ionization of triphenylmethyl chloride to form carbonium ion, which determines the overall rate of the process, is common to both reactions.

$$\text{I (a) } R{-}Cl \xrightarrow{\text{Slow}} R^+ + Cl^-$$

$$\text{(b) } R^+ + CH_3OH \xrightarrow{\text{Fast}} R{-}OCH_3 + H^+$$

$$\text{II (a) } R{-}Cl \xrightarrow{\text{Slow}} R^+ + Cl^-$$

$$\text{(b) } R^+ + C_6H_5CH_2OH \xrightarrow{\text{Fast}} R{-}OCH_2C_6H_5 + H^+$$

The second stage (*b*) in which the carbonium ion reacts with methanol or benzyl alcohol molecules is fast and should have no influence upon the kinetics of the process.

A second experimental fact which is not in agreement with the simple $S_N1$ scheme is that perchlorate ion strongly catalyzes the alcoholysis of triphenylmethyl chloride, but does not at all accelerate the reaction of triphenylmethyl chloride with chloride ion ($\overset{*}{Cl}^-$) or azide ion.

To account for the new experimental data, Ingold suggests the following scheme of alcoholysis according to $S_N1$ mechanisms:

$$R{-}Cl \xrightarrow[\text{Slow}]{(a)} R^+Cl^- \xrightarrow[\text{Fast}]{(b)} (R^+Cl^-)(HOR') \begin{cases} \xrightarrow[\text{Fast}]{i} R{-}Cl \\ \xrightarrow[\text{Fast}]{j} R{-}O{-}R' \end{cases}$$

The above scheme shows that the alcohol molecule participates in the intermediate stage, but enters into it in the rapid stage of the reaction. The yield of the ether ROR′ depends on the ratio $j/(i+j)$ which differs for different alcohols.

At low alcohol concentrations the rate of alcoholysis may be considered (with some approximation) independent of the alcohol concentration. At higher concentrations the catalytic effect of alcohol as a polar compound begins to tell.

Therefore, *the first principal addition by Ingold to the $S_N1$ mechanism consists in that the molecule of the nucleophilic reagent enters the activated complex.*

However this addition by itself does not yet explain the above-mentioned selective catalytic effect of perchlorate ion.

And Ingold makes a second addition: he comes to the conclusion *that not only the ionization stage determines the kinetics of the reaction. There must be a second stage, which also influences the overall kinetics of the process.* Otherwise, for example, the catalytic effect of perchlorate ion should have been the same for the alcoholysis of triphenylmethyl chloride and for the reaction with $\overset{*}{Cl}^-$ and $N_3^-$ because according to the simple $S_N1$ mechanism the slow stage of all these reactions is common (ionization with formation of a triphenylmethyl cation).

In examining the isotopic exchange of triphenylmethyl chloride with the chloride of a quaternary ammonium salt, Ingold assumed that stage (*d*) of formation of the final product $R\overset{*}{Cl}$ is reversible to some extent,

$$R{-}Cl \xrightarrow{(a)} R^+Cl^- \xrightarrow{(b)} (R^+Cl^-)(R_4\overset{+}{N}\overset{*}{Cl}^-) \begin{cases} \xrightarrow{(d)} (R\overset{*}{Cl}) \\ \xrightarrow{(c)} (RCl) \end{cases}$$

this accounting, for instance, for the fact that the ratio $d/(c+d)$ is generally slightly less than one half. The two substances $R\overset{*}{Cl}$ and RCl have the same chemical properties. Therefore, if the assumption of reversibility is true, there must exist alongside the intermediate complex $(R^+Cl^-)\cdot(R_4\overset{+}{N}\overset{*}{Cl}^-)$, a stereoisomeric quadrupole $(R^+\overset{*}{Cl}^-)\cdot(R_4\overset{+}{N}Cl^-)$. There should be a transition between these two quadrupoles, for example, through a complex of the type $Cl\cdots R\cdots\overset{*}{Cl}$.

*It is this quadrupole isomerization that Ingold considers the second slow stage of reactions proceeding according to the $S_N1$ mechanism.*

Ingold ascribes various structures to the intermediate stage arising on rearrangement of the quadrupole. Thus, in the case of

anionic isotopic exchange he considers it the aggregate of the carbonium ion and the tripole $Cl^-R_4\overset{+}{N}\overset{*}{C}l^-$:

$$\left\{ \begin{matrix} & R^+ & \\ Cl^- & R_4\overset{+}{N} & \overset{*}{C}l^- \end{matrix} \right\}$$

In the case of alcoholysis it is a complex of the carbonium ion with the rest of the molecule linked to the alcohol molecule by a hydrogen bond:

$$R^+\{Cl\cdots H-O-R'\}$$

At present, the general scheme of reactions of isotopic anionic exchange and alcoholysis, which proceed according to $S_N1$ mechanisms, may be represented according to Ingold as follows:

$$R-Cl \underset{\text{Fast}}{\overset{\text{(a) Slow}}{\rightleftharpoons}} R^+Cl^- \underset{\text{Fast}}{\overset{\text{(b)}}{\rightleftharpoons}} \left\{ \begin{matrix} R^+Cl^- \\ R_4\overset{+}{N}X^- \end{matrix} \right\} \underset{\text{Slow}}{\overset{\text{(c)}}{\rightleftharpoons}}$$

$$\rightleftharpoons \left\{ \begin{matrix} R^+X^- \\ R_4\overset{+}{N}Cl^- \end{matrix} \right\} \underset{\text{Fast}}{\rightleftharpoons} R^+X^- \underset{\text{Slow}}{\overset{\text{Fast}}{\rightleftharpoons}} R-X$$

$$R-Cl \overset{\text{(a)}}{\rightleftharpoons} R^+Cl^- \overset{\text{(b)}}{\rightleftharpoons} \left\{ \begin{matrix} R^+Cl^- \\ HOR' \end{matrix} \right\} \overset{\text{(c)}}{\rightleftharpoons} \left\{ \begin{matrix} R^+ + {}^-OR \\ H^+Cl^- \end{matrix} \right\} \rightleftharpoons R^+ \ {}^-OR \rightleftharpoons ROR'$$

The energy scheme of the process, according to Ingold, is as follows: the total energy of the process is equal to the endothermic ionization energy (stage *a*) minus the exothermic energy of dipole association (stage *b*) plus the activation energy of quadrupole isomerization (stage *c*).

The catalytic effect of polar molecules consists in that they lower the energy of the first, slow stage, viz., the ionization stage, and affect dipole association and quadrupole isomerization in the direction of lowering the total energy of activation.

As was mentioned before, perchlorate ion strongly catalyzes the alcoholysis of triphenylmethyl chloride but does not accelerate the reaction of anion exchange of triphenylmethyl chloride with the chloride anion ($\overset{*}{C}l^-$) and the azide anion ($N_3^-$).

Ingold accounts for these facts as follows: since the first, slow (ionization) stage is the same for both reactions, it is natural to assume that the perchlorate ion participates in the second slow stage of the process.

In the case of anionic exchange $ClO_4^-$ is included in the intermediate complex, apparently by substitution of the chloride ion. This should result in an energetically equivalent quadrupole ($R^+Cl^-$) ($R_4\overset{+}{N}ClO_4^-$) from which, however, the end product of the reaction cannot form. Ingold considers that though the formation of such

a quadrupole (involving temporary seizure of carbonium ion $R^+$) should retard the reaction somewhat, in benzene solution this deceleration is so slight that it cannot be detected experimentally.

The catalytic effect of perchlorate ion on alcoholysis, according to Ingold, appears to be a much more complex process.

When the quadrupole $(R^+Cl^-)(R'OH)$, containing a molecule of alcohol, is attacked by perchlorate ion, the latter can replace only the chloride ion in the ionic pair $R^+Cl^-$. Ingold ascribes to the intermediate complex formed the structure of a tripole ion $ClO_4^-R^+\begin{pmatrix}Cl\\H\\OR'\end{pmatrix}^-$, which binds a molecule of hydrogen chloride in the complex anion component $(Cl\cdots H\cdots OR')$. This "loss" of HCl means that only an ether $R-O-R'$ can form from the above tripole intermediate but not chlorine derivative $R-Cl$. This explains the strong catalytic effect of perchlorate ion on the alcoholysis of triphenylmethyl chloride. The addition of chloride ions suppresses this catalytic effect because of the redisplacement of perchlorate ion from the complex by chloride ion to form the original quadrupole $(R^+Cl^-)(HOR')$, or, if chloride ion is present in excess, of the quadrupole $(R^+Cl^-)(R_4^+NCl^-)$.

As was stated earlier (p. 132), Swain, while studying the reaction between methyl bromide and pyridine in benzene (as an example of an $S_N2$ reaction) came to the conclusion that it also follows the termolecular mechanism.

This study of Swain was repeated by Pocker [43], a coworker of Ingold's. Like Swain, he found that the reaction is a second-order reaction: first-order with respect to methyl bromide and first-order with respect to pyridine.

It was found that the catalytic effect of additions of polar substances on this reaction was much weaker than in $S_N1$ reactions (such as alcoholysis of triphenylmethyl chloride). Having studied the effect of additions of methanol, benzyl alcohol, phenol and nitromethane, Pocker showed that the relation of the reaction rate to the concentration of the substance added is not linear.

On these grounds he concluded that Swain's opinion as to the termolecular nature of the reaction between methyl bromide and pyridine in benzene is erroneous.

It should be noted that on the question of the mechanism of $S_N2$ reactions the basic difference between Swain's and Ingold's views consists in the following: Swain considers that the intermediate state involves a third molecule (besides the two molecules of reagent), that of the polar substance added or even (if nothing is added) of the nonpolar solvent; reactions of this type should, consequently, have a definite kinetic order with respect to the additives.

But Ingold thinks that the additive molecules do not participate in the intermediate state. Their catalyzing effect is due to the fact that the dipoles of the added molecules stabilize the intermediate stage which is more polar than the initial stages of the molecules. In this case, naturally, no definite kinetic order with respect to the added substance could be expected.

A number of convincing confirmations of the existence of the $S_N2$ mechanism were obtained by Ingold and coworkers* when studying the Finkelstein substitution reaction ($RX + LiI \rightleftarrows RI + LiX$) from the point of view of steric, polar and entropy factors [45, 46].

Until 1948 the concepts of the two mechanisms of nucleophilic substitution at the saturated carbon atom were sufficiently simple and in quite satisfactory agreement with available facts.

The new experimental data obtained in the study of nucleophilic substitution in benzene, nonpolar inert medium, brought up new hypotheses. This refers particularly to the $S_N1$ mechanism, which became much more complex. Besides, it must be kept in mind that Ingold's modernized $S_N1$ mechanism shown schematically on page 137 can by no means be regarded as proved. All the fine points of the mechanism of nucleophilic substitution reactions—the structure of activated complexes, the mechanism of the influence of additions, the effect of the solvent—have still to be solved.

### 2-2.2 Homolytic Substitution

Reactions of this type include such important processes as the halogenation of saturated hydrocarbons in the presence of light, sulphochlorination, nitration of saturated hydrocarbons, as well as certain reactions between acyl peroxides and cycloolefins containing an active methylene group, reactions of free radicals with alkanes, etc., following the general scheme:

$$\left.\begin{array}{l} Z\cdot + R\!:\!X \longrightarrow R{-}Z + \cdot X \\ \text{or} \\ Y\!:\!Z + R\!:\!X \longrightarrow R{-}Z + Y{-}X \end{array}\right\} S_R$$

The concept of homolytic substitution is broader than that of free-radical substitution and includes the latter. The participation of free radicals as kinetically independent particles is characteristic of free-radical substitution. Of the two examples of homolytic substitution given above the first is a free-radical reaction.

---

* It must not be concluded from this, however, that the termolecular (push-pull) mechanism is in general impossible.

All the presently known reactions of radical substitution at the saturated carbon atom are evidently chain processes. For example, methane chlorination in the presence of light takes place according to the following scheme:

$$Cl\!:\!Cl \xrightarrow{h\nu} 2Cl\cdot$$

$$Cl\cdot + CH_4 \longrightarrow CH_3\cdot + HCl$$

$$CH_3\cdot + Cl\!:\!Cl \longrightarrow CH_3Cl + Cl$$

Further chlorination of $CH_3Cl$ up to $CCl_4$ also proceeds according to a chain mechanism.

Products of recombination of methyl radicals ($C_2H_6$) are practically absent because of the great length of the chain ($10^5$-$10^6$ links).

Nitration of saturated hydrocarbons and of the side chains of alkylaryl hydrocarbons by nitrogen oxides or by dilute nitric acid at high temperatures proceeds according to the following mechanism [47, 48, 49]:

$$R\!:\!H + \cdot NO_2 \longrightarrow R\cdot + HNO_2$$

$$R\cdot + \cdot NO_2 \longrightarrow R{-}NO_2$$

$$HNO_2 + HNO_3 \longrightarrow H_2O + 2\cdot NO_2 \quad \text{etc.}$$

Esters of nitrous acid may form as by-products:

$$\cdot NO_2 \longrightarrow \cdot O{-}NO$$
$$R\cdot + \cdot O{-}NO \longrightarrow R{-}ONO$$

It should be noted that replacement by the nitro group becomes easier from the primary hydrogen (in the methyl group) to the secondary (in the $-CH_2$ group) and is the easiest with the tertiary (in the $\diagup\!\!\diagdown CH$ group).

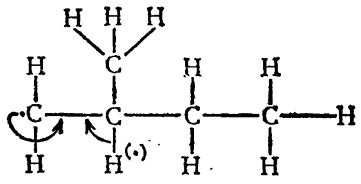
Other reactions of radical substitution at the saturated carbon atom (halogenation, sulphochlorination, oxidation) give a similar picture.

The reason for this phenomenon may be explained as follows: the first stage of all these reactions consists in the breaking off of a hydrogen atom from the hydrocarbon by the radical reagent.

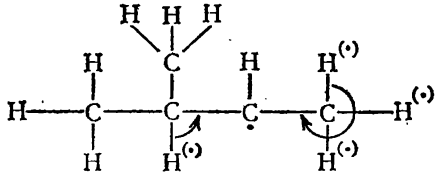
$$A\cdot + H\!:\!R \longrightarrow AH + \cdot R$$

It is obvious that the direction of this stage of the reaction (which of the hydrogens is broken off by the radical reagent) should depend essentially on the energy of the free radical formed.

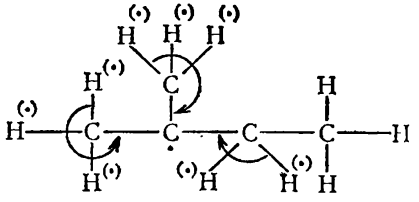
Consider, for example, the three free radicals which may form when a hydrogen atom is removed from the isopentane molecule:



(I)



(II)



(III)

As the presence of a localized electron on a carbon atom calls for a large amount of energy (and consequently for instability of the free radical), of the three radicals shown above, that possessing the least energy will have the greatest probability of conjugating its odd electron with the σ electrons of α-C — H bonds (see page 191). The C — C bonds are much less capable of conjugation with an odd electron than C — H bonds.

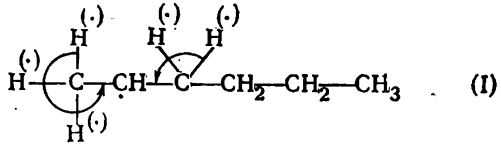
In radical I the odd electron conjugated with the σ electrons of one α-C — H bond, in radical II, with the σ electrons of four α-C — H bonds, and in radical III, with the σ electrons of eight α-C — H bonds. Hence, radical III possesses the lowest energy, because in it the odd electron is the least localized on the carbon atom; eight of the hydrogen atoms are also of a radical nature (to at least the slightest extent). Because of this, radical III would form more readily from isopentane than the other two radicals. This is why the tertiary hydrogen can be replaced easier than the secondary or the primary one. Similarly, it can be readily under-

stood why a secondary hydrogen atom is replaced more easily than a primary and less easily than a tertiary one.

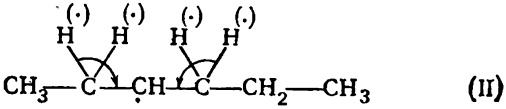
In the case when a normal alkane having several methylene groups, such as *n*-hexane, is used in a reaction of radical substitution (for instance, nitration), substitution should be expected to take place predominantly at the second carbon atom:

$$CH_3-CH_2-CH_2-CH_2-CH_2-CH_3 \xrightarrow{HNO_3} CH_3-\underset{\displaystyle NO_2}{\underset{|}{CH}}-CH_2-CH_2-CH_2-CH_3$$

This assumption stems from a comparison of the energies of the two possible radicals which may form when one of the secondary hydrogens of hexane is split off:



(I)



(II)

Radical I is stabilized by conjugation of the odd electron with 5 α-C—H bonds to a somewhat greater extent than radical II, where the odd electron is conjugated with four α-C—H bonds. As a result of this, radical (I) should possess less energy and form more easily than radical (II).

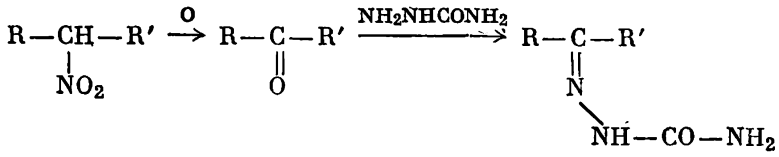
Until very recently, for over fifty years it was thought that nitration of normal alkanes after Konovalov actually proceeds predominantly or even exclusively at the second carbon atom. This conclusion was derived from Konovalov's work [50], as well as from that of other workers [51].

Recently [52-55] this conclusion was proved to be wrong and it was established that in the nitration of normal alkanes a mixture of approximately equal quantities (to ~5%) of all the possible secondary nitro compounds formed.

Apparently, unlike the possible free radicals of isopentane (I, II and III, page 141), the energies of the radicals of types I and II of normal alkanes differ insignificantly, and if slightly more 2-nitroalkane does form, this excess does not amount to more than 5% over the quantities of the other isomers formed.

The prolonged misconception about the exclusive formation of 2-nitro derivatives was due to a combination of systematic experimental errors. The conclusion that only 2-nitroalkane was present in the reaction mixture was

derived from the following reactions:

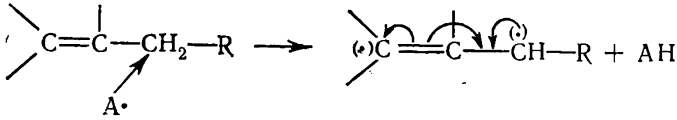


The result was invariably semicarbazone of a methylalkyl ketone and hence the conclusion that the nitro group is located exclusively at the second carbon atom.

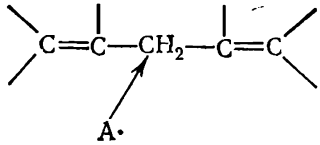
It was shown, however, that oxidation of different secondary nitro compounds to ketones proceeds at different rates; 2-nitroalkane oxidizes several times faster than the other isomers.

Further, of all the ketones formed the fastest to react with semicarbazide (and hydroxylamine) is methylalkyl ketone, and finally, the semicarbazide of the methylalkyl ketone possesses the lowest solubility. Thus, at all the stages the reaction mixture became enriched in the substance with the functional group in the 2 position, while the other isomers were lost.

In the above examples the free radical is stabilized due to conjugation of the odd electron with σ electrons (of C—H bonds). The free radical may be stabilized still more by conjugation of the odd electron with π electrons. This accounts for the increased reactivity of the "allylic position" manifested by the fact that free radicals generally replace the "allylic hydrogen" and do not add to the double bond:



The methylene group is particularly sensitive to radical reagents when situated between two double bonds



because the radical formed in the first stage of the reaction is stabilized by the conjugation of the odd electron with the π electrons of two double bonds:

$$-CH=CH-\dot{C}H-CH=CH-$$

A characteristic trait of radical reactions is that a radical reagent reacting with a saturated molecule attacks only one of the *peripheral* atoms.

Thus, a free methyl and other hydrocarbon radicals will react in the gas phase with alkanes and other saturated organic molecules removing a hydrogen from the periphery of the molecule without interfering with the carbon skeleton. The reaction

$$CH_3\cdot + CH_3-C_nH_{2n+1} \longrightarrow CH_3-CH_3 + \cdot C_nH_{2n+1}$$

is more difficult to accomplish than the reaction:

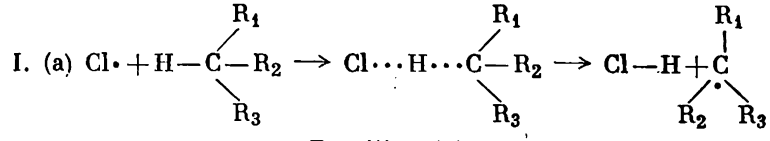
$$CH_3\cdot + C_nH_{2n+2} \longrightarrow CH_4 + \cdot C_nH_{2n+1}$$

in spite of the fact that the energy of the C — C bond (58.6 kcal/mole) is lower than that of the C — H bond (87.3 kcal/mole).

Reactions in solution indicate that the steric factor may be decisive in determining the direction of reactions of active free radicals. If atomic hydrogen, which is very small in size, can cause rupture of a C — C bond in the reaction with alkanes the larger methyl radical can remove only peripheral, i.e., hydrogen, atoms from the molecule it collides with.

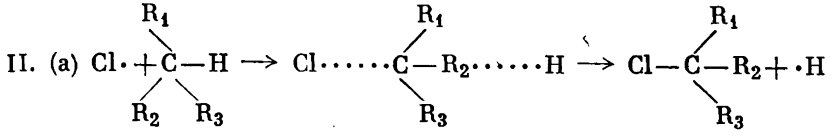
The stereochemistry of radical substitution has been studied much less than that of nucleophilic substitution.

The first paper in this field was published by Kharasch, Brown and Chao [56]. They studied the stereochemistry of the reaction of atomic halogenation, found racemization and concluded on these grounds that the reaction of halogenation passes through a stage of intermediate formation of free hydrocarbon radicals. Their proof consists in the following. Two probable reaction mechanisms illustrated by schemes I and II were considered:



Transition state

(b) $R_1R_2R_3C\cdot + Cl_2 \longrightarrow R_1R_2R_3C-Cl + \cdot Cl$



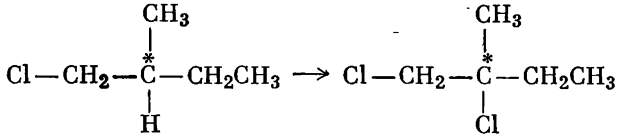
Transition state

(b) $H^\cdot + Cl_2 \longrightarrow HCl + \cdot Cl$

When the reaction proceeds according to scheme I, a free radical $R_1R_2R_3C\cdot$ having a planar configuration is formed; if an optically active hydrocarbon $R_1R_2R_3CH$ is assumed, a racemic mixture should result.

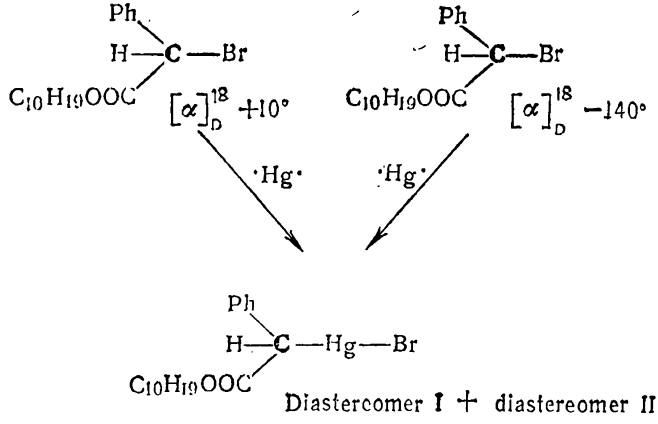
If the reaction proceeds according to scheme II, the substitution ıould proceed with inversion of configuration and form an optically ;tive product.

If optically active 1-chloro-2-methylbutane is chlorinated to ,2-dichloro-2-methylbutane



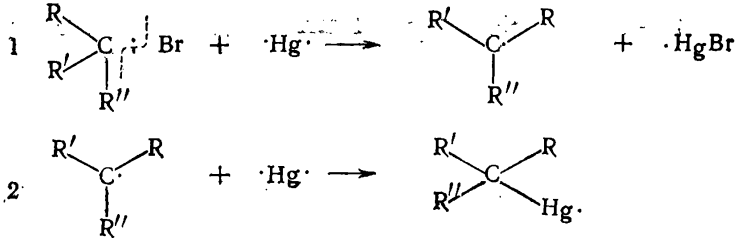
hether photochemically or with sulphuryl chloride and benzoyl eroxide, an optically inactive substance results. This is the proof ıat atomic halogenation follows scheme I.

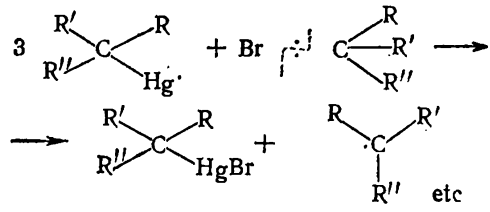
The authors mentioned above base their proof on the premise ıat the free radical has a flat configuration. The stereochemistry f the reactions of halogen derivatives with metallic mercury con- rms this premise. Thus both diastereomers of the *l*-menthyl ester f α-bromomercuricphenylacetic acid react with metallic mercury t room temperature yielding the same mixture of organomercury iastereomers [57].



Diastereomer I + diastereomer II

The mechanism of this reaction may be represented by the fol- ıwing general scheme:



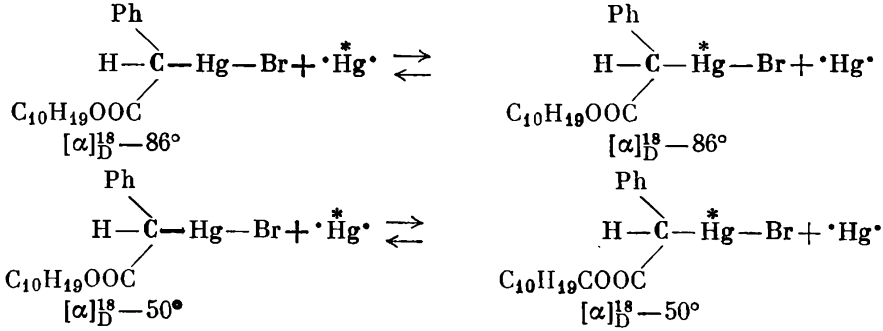


The stereochemical result of this reaction—racemization in the case of both diastereomeric bromides—can be accounted for only by assuming that the free radical intermediates $RR'R''C\cdot$ formed in stage 1 have a planar conformation.

Occurrence of homolytic substitution at the saturated carbon atom without racemization indicates, as a rule, that no free radicals are formed as kinetically independent particles.[1]

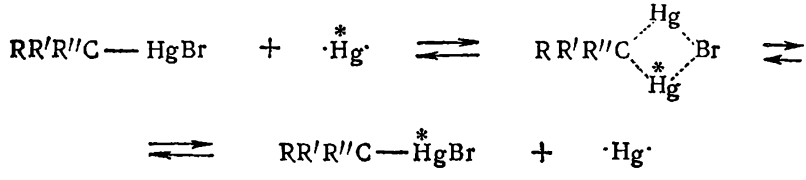
An example of such a homolytic, but not free-radical, reaction is the reaction of isotopic exchange of the two diastereomers of *l*-menthyl ester of α-bromomercuricphenylacetic acid with metallic mercury labeled with the radioactive isotope $^{203}Hg$.

This reaction proceeds readily at room temperature with strict retention of stereochemical configuration [59].



The angles of rotation of the diastereomers before the reaction remain unchanged after establishment of isotopic equilibrium.

The mechanism of the isotope exchange reaction under consideration can probably be represented by the following scheme [60]:



[1] Exceptions are some free radicals of bicyclic systems, which retain their configuration because of rigidly fixed valences [58].

Thus, so far only two stereochemical results have been ascertained or homolytic substitution at the saturated carbon atom: racemiation (free-radical chain reaction) and retention of configuration.

### 2-2.3 Electrophilic Substitution

Reactions of electrophilic substitution at the saturated carbon atom include reactions following the scheme:

$$\left.\begin{array}{l} Z^+ + R{:}\,X \longrightarrow R{-}Z + X^+ \\ Y{:}\,Z + R{:}\,X \longrightarrow R{-}Z + X{-}Y \end{array}\right\} S_E$$

Several types of electrophilic substitution at the saturated carbon atom are shown below.

*Isotopic exchange of hydrogen for deuterium or tritium*

$$R{-}H + D^+ \rightleftarrows R{-}D + H^+$$

$$R{-}H + T^+ \rightleftarrows R{-}T + H^+$$

*Exchange reactions of organometallic compounds with salts of other metals*

$$R{-}MeX_{n-1} + Me'X_m \longrightarrow R{-}Me'X_{m-1} + MeX_n$$

A particular case of reactions of this type is the isotopic exchange reaction (Me'— isotope of Me; $n = m$).

*Substitution of the metal in organometallic compounds by hydrogen*

$$R{-}Me + H^+ \longrightarrow R{-}H + Me^+$$

A concrete example of reactions of this type is the reaction of organomagnesium compounds with water or acids, e.g.:

$$R{-}CH_2{-}MgBr + H{-}Br \longrightarrow R{-}CH_2{-}H + MgBr_2$$

Metalation is another reaction of this type:

$$C_6H_6 + CH_3{-}CH_2{-}Na \longrightarrow C_6H_5Na + CH_3{-}CH_3$$

$$CH_3{-}C{\equiv}C{-}H + CH_3{-}CH_2{-}MgBr \longrightarrow CH_3{-}C{\equiv}C{-}MgBr + CH_3{-}CH_3$$

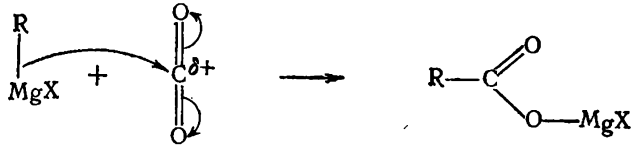
*Substitution of halogen for metal*

$$R-Me+X^+ \longrightarrow R-X+Me^+$$

The reactions of organolithium and organomercury compounds with bromine may serve as examples.

The electrophilic reaction of organomercury compounds proceeds readily in the presence of catalysts (pyridine, halogen salts of certain metals), which facilitate the heterolytic rupture of the halogen molecule. In the absence of such catalysts a radical reaction may predominate.

*Carbonation of organometallic compounds*



Carbonation of organometallic compounds is a reaction of electrophilic substitution at the carbon atom linked with the metal.

*Decarboxylation of silver salts of carboxylic acids by reactions with bromine*

$$R-C(=O)-O-Ag+Br:Br \longrightarrow R-Br+CO_2+AgBr$$

Decarboxylation of carboxylic acids proper is also an electrophilic substitution at the carbon atom

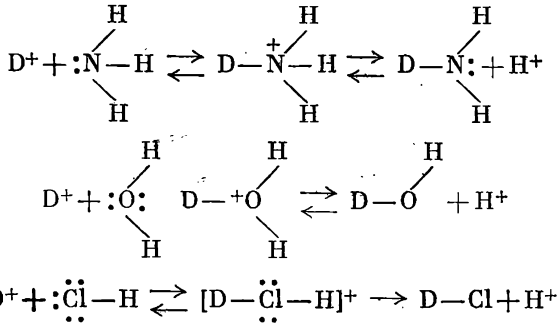
$$R-C(=O)-O-H \longrightarrow R-H+CO_2$$

**Splitting of Carbon-Carbon Bonds.** Splitting of carbon-carbon bonds by electrophilic substitution is observed in some special cases under the influence of proton-donor substances:

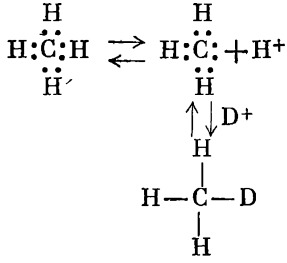
$$R'-C(R'')-C(O^-Me^+)-C(R''')(R'''')-R+B:H \longrightarrow R'-C(R'')-H+R'''R''''C=O+BMe$$

Of all the types of reactions given above, the most thoroughly investigated are the mechanisms of reactions of deuteroexchange and of exchange reactions of organometallic compounds.

**Deuteroexchange Reactions.** Substitution of deuterium for hydrogen linked to carbon is more difficult than for hydrogen linked to nitrogen (trivalent), oxygen or halogen. This is due to the fact that the molecules of $NH_3$, $H_2O$, and HCl possess free electron pairs to which a deuterium ion attaches readily, a hydrogen ion being released simultaneously or subsequently from another electron pair [34]:



A saturated carbon atom, however, has no free electron pair and elimination of the hydrogen has to precede (or accompany) the addition of the deuterium:



Rupture of the C — H bond requires a large amount of energy, so that this process takes place only if hydrogen elimination is facilitated by a catalyst or if the C — H bond is weakened by the presence of activating groups.

In aliphatic compounds the exchange of hydrogen for deuterium generally proceeds as an ionic reaction by one of the following two schemes:

$$(1)\quad R{-}H + D{-}A \rightleftarrows [RHD]^+ + A^- \rightleftarrows RD + HA$$

$$(2)\quad R{-}H + D{-}A \rightleftarrows R^- + [HDA]^+ \rightleftarrows RD + HA$$

In the first scheme deuterium adds to the organic compound RH to form a carbonium ion $[RHD]^+$, the decomposition of which

may result in re-formation of the initial RH, as well as in the formation of RD.

According to the second scheme the deuterating agent DA removes a proton from the organic compound, resulting in the onium cation $[HDA]^+$ and the organic anion $R^-$. If $R^-$ later removes a deuteron from the onium ion an exchange ensues, resulting in the formation of RD.

If D — A is a stronger base than RH, the exchange follows scheme (1); if, conversely, D — A is a weaker base than RH, the exchange follows scheme (2).

Hydrogen atoms in aliphatic compounds may be exchanged for deuterium by the action of heavy water in the presence of acidic or basic catalysts. However, basic catalysts are more typical of such reactions, because bases facilitate the removal of proton from the reacting molecule:

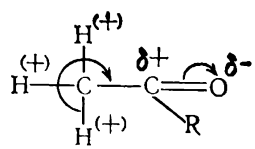
$$R{-}H + B \longrightarrow R{:} + BH^+;$$
$$R{:} + D_2O \longrightarrow R{-}D + OD^-$$

This is the mechanism, for instance, of the exchange catalyzed by bases in the C — H bonds of the molecules $CH_3 - CONH_2$, $CH_3 - C \equiv N$, $CH_3 - CH_2 - NO_2$, etc.

Electronegative substituents may be arranged in the following sequence of effectiveness in facilitating exchange in aliphatic compounds:

$$-NO_2 > \begin{matrix} \diagdown \\ C{=}O \\ \diagup \end{matrix} > C \equiv N > -\begin{matrix} O \\ \| \\ C \\ \diagdown \\ O^- \end{matrix} > \begin{matrix} O^- \\ \diagdown \\ S{-}O \\ \diagup \\ O^- \end{matrix} > Cl$$

The influence of the substituents indicated is due to the fact that they attract the $\sigma$ electrons of the $\alpha$-C — H bonds, e.g.:

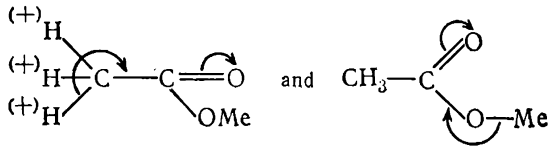


As a result, the $\alpha$-hydrogen atoms are more inclined to protonize than in the absence of a substituent. On the other hand, alkyl (and some other) groups impede exchange.

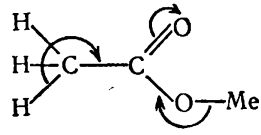
Rather interesting results were obtained by Miklukhin [35] in an investigation of acetate exchange. The nature of the metal was found to have a strong influence on the rate of exchange. Exchange is much more rapid in lead, mercury and cadmium than in barium, calcium or sodium acetates. Thus at 160° the exchange takes 7

hours to reach 50% in $(CH_3COO)_2Pb$, 25 hours to reach it in $(CH_3COO)_2Hg$, 54 hours in $(CH_3COO)_2Cd$, 240 hours in $(CH_3COO)_2Ba$ and $(CH_3COO)_2Ca$ and 150 hours in $CH_3COONa$.

The reason for this behaviour may be that competitive conjugation is possible in acetate molecules between the H — C and the C = O bonds, on one hand, and Me — O and C = O bonds, on the other




In the case of strongly electropositive metals (such as Na, Ca, Ba) which form a polar bond with oxygen conjugation occurs mainly between the Me — O and C = O bonds; the σ electrons of the C — H bonds do not participate in this conjugation to any appreciable extent, so that the methyl group hydrogens are "mobilized" very little and are difficult to replace:

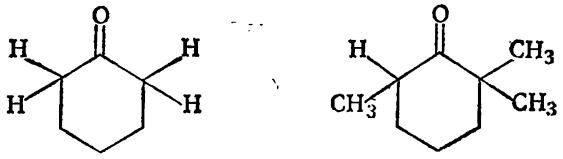



On the contrary, the presence of metals such as Pb and Hg which form bonds of low polarity with oxygen (close to covalent)*, weaken the conjugation of the Me — O and C = O bonds and thus strengthen the H — C and C = O bonds. The hydrogen atoms in the molecules of such salts are more mobile and are much easier to exchange.

Characteristic examples of the influence of σ, π conjugation of bonds on the rate of the deuteroexchange were studied by Nesmeyanov, Kursanov and coworkers [63].

They discovered that at 130° in the presence of $K_2CO_3$ only α-hydrogen atoms were exchanged with heavy water in the molecules of cyclic ketones (in 50-70 hours).

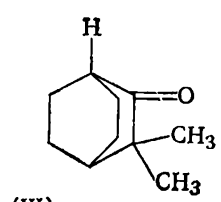
Thus, all four α-H in cyclohexanone (I), and the only α-H in 2,2,6-trimethylcyclohexanone (II) were exchanged.



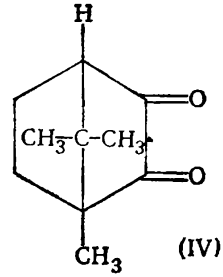

(I) (II)

* The electronegativities of these metal atoms are: Na—0.9; Ba—0.9; Ca—1.0; Cd—1.5; Pb—1.8; Hg—1.9.

In the molecules of camphenilone (III) and camphorquinone (IV) σ,π conjugation is impossible because of steric hindrance (the axis of the C — H bond is not in the plane of the π electrons of the C = O group). Therefore despite the presence of α-hydrogen atoms neither of these substances react with heavy water.




(III)




(IV)

Several examples of the influence of bond conjugation on deuteroexchange in acyclic aldehydes and ketones have been described [64, 65].

Saturated hydrocarbons do not, as a rule, participate in deuteroexchange reactions. Exceptions are alkanes possessing tertiary carbon atoms. Deuteroexchange of such hydrocarbons was discovered and studied almost simultaneously by Kursanov and coworkers [66] and by Stevenson and coworkers [67].

Both groups of workers suggested a similar mechanism of exchange, namely the formation of carbonium ions, as a result of oxidation of the methine group by sulphuric acid, followed by a chain reaction with the participation of the carbonium ion.

Kursanov [66, 72] investigated the hydrogen exchange of saturated hydrocarbons by the action of sulphuric acid monohydrate enriched with deuterium at 20-25°. Results are given in Table 2-3.

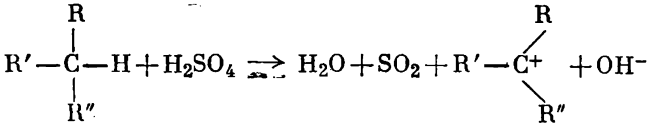
TABLE 2-3

| Hydrocarbon | Time in hours | Exchange, % | Number of tertiary carbon atoms |
|---|---|---|---|
| *n*-Heptane | 50 | 2 | 0 |
| *n*-Dodecane | 4 | 1 | 0 |
| 2,2-Dimethylhexane | 4 | 2 | 0 |
| Cyclohexane | 3 | 1 | 0 |
| 1,1-Dimethylcyclohexane | 4 | 2 | 0 |
| 3-Methylheptane | 5 | 97 | 1 |
| 3-Methylhexane | 11 | 96 | 1 |
| 2,2,3-Trimethylbutane | 25 | 100 | 1 |
| 2,2,4-Trimethylpentane | 25 | 93 | 1 |
| Methylcyclohexane | 0.5 | 99 | 1 |

It is evident from the table that hydrocarbon molecules having only primary, secondary and quaternary carbon atoms are incapable of exchange. But if the molecules have at least one tertiary carbon atom, hydrogen exchange takes place, and not only the hydrogens at the tertiary carbon atom participate in the hydrogen exchange, but all the rest of the hydrogen atoms in the molecule as well.

The following suggestions have been made concerning the mechanism of the reaction.

The first stage of the reaction consists in oxidation of the methine group by sulphuric acid* to form a carbonium ion



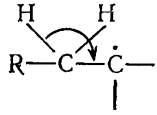
After this the process follows a chain reaction mechanism, because the number of exchanged molecules greatly exceeds the number of oxidized molecules. Thus, the hydrogen exchange of hydrocarbons under the influence of sulphuric acid goes through the following stages.

1. *Initiation of the chain.* This stage consists in the formation of oxidized particles (ions). During their short lifetime these particles exchange their hydrogen atoms to a greater or lesser extent for deuterium**.

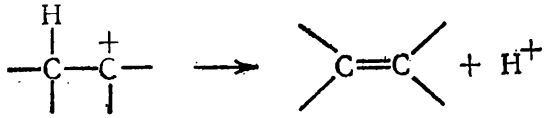
---

* This assumption is confirmed by the following facts: (a) non-oxidizing acids ($CH_3COOH$, $H_3PO_4$, HCl) do not cause exchange in the absence of catalysts; (b) in a number of experiments the presence of the product of reduction of sulphuric acid, $SO_2$, was established; (c) methine groups of hydrocarbons are generally the points of attack by oxidizing agents.

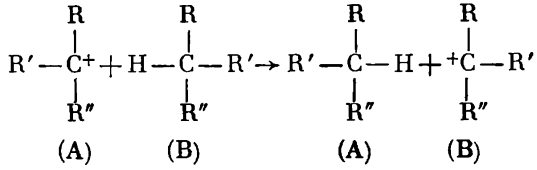
** Carbonium ions should enter into the exchange reaction because the positive charge should increase the proton mobility of α-hydrogen atoms:



This is confirmed, for example, by the tendency of carbonium ions to form alkenes:



2. *Propagation of the chain*, i.e., transfer of the active cationic centre of one particle (*A*), the hydrogen atoms of which have already been exchanged for deuterium, to another molecule (*B*), which does not yet contain deuterium:



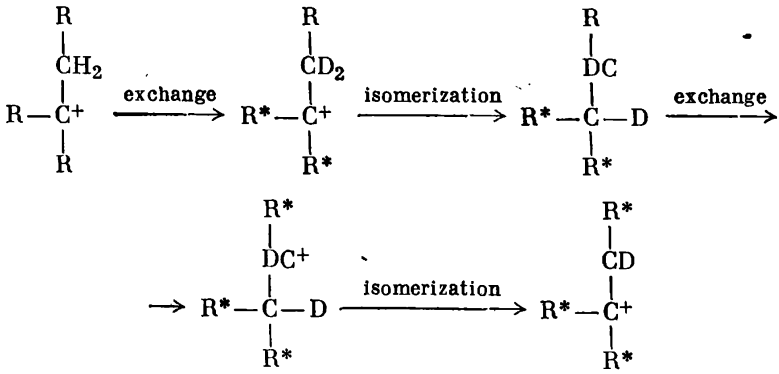

3. *Termination of the chain.* The concluding stage of the reaction is chain termination, which occurs in the usual manner (recombination of the carbonium ion with some anion, such as $OH^-$).

Papers have been published [67, 68] in which other versions of the mechanism of exchange in hydrocarbons with tertiary carbon atoms are described.

In the carbonium ion only the α-hydrogen atoms are exchanged. Participation of the other hydrogen atoms in the exchange is due to the fact that propagation of the chain is accompanied by simultaneous isomerization of the carbonium ions owing to transfer of the hydride ion.[1] As a result, the positive charge migrates along the hydrocarbon chain.

According to Stevenson, the hydride ion can migrate from a tertiary carbon atom only to a tertiary carbon, so that all the hydrogen atoms are exchanged except one tertiary hydrogen atom.

According to Kursanov, migration is possible not only to the tertiary, but to other atoms of the carbonium ion as well, e.g.

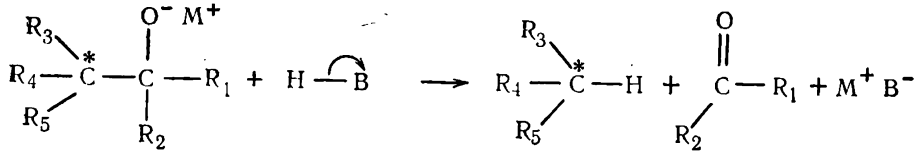



[1] Such isomerization in the exchange has been proved experimentally [67, 70]. Isomerization of a propyl cation of the type $CH_3—CH_2—{}^{14}CH_2^+ \rightleftarrows {}^+CH_2—CH_2—{}^{14}CH_3$ was proved in the reaction of *n*-propylamine perchlorate with nitrous acid [71].

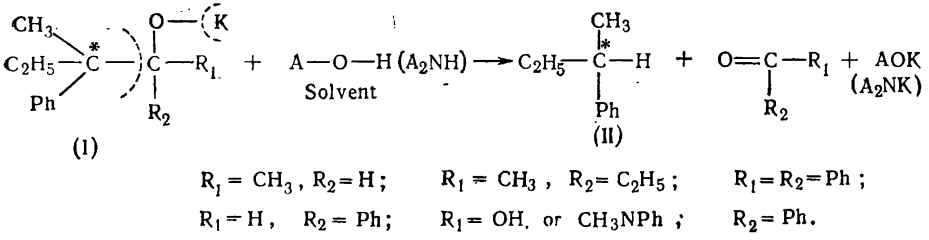
The stereochemistry of the deuteroexchange depends to a great extent on the medium in which the reaction is carried out (see below).

**Electrophilic Exchange of Carbon for Hydrogen.** Cram [73-80] investigated the stereochemistry of electrophilic substitution of hydrogen for carbon at the saturated carbon atom.

The reactions studied by him may be illustrated in general form by the following scheme:



For example, five compounds of type I when heated in different solvents (which are sources of protons) split to form 2-phenylbutane (II) and the corresponding ketone (acid or amide):

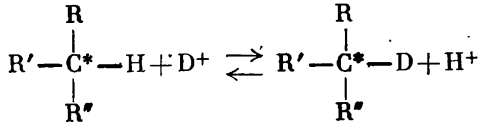


(Compounds I were obtained from optically pure methylethylphenylacetic acid.)

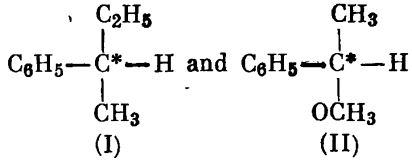
It is readily perceived that the reaction under consideration is the reverse of aldol condensation. The stereochemical course of this reaction depends on the nature of groups $R_1$ and $R_2$, but still more on the nature of the solvent. As a rule, in weakly ionizing solvents, such as tertiary alcohols, and in the presence of metal alcoholates as catalysts, retention of configuration predominates. Apparently an $S_E2$ reaction takes place in this case. In strongly ionizing solvents, which are not proton donors, such as dimethylsulphoxide, predominant racemization is observed. Cram attributes this to the fact that carbanions formed in a highly polar medium exist long enough to solvate uniformly (on both sides). In strongly ionizing proton-donor solvents, such as diethyleneglycol, predominant inversion is observed. Cram thinks that under these conditions carbanions exist a much shorter time and are attacked by protons before the screening effect of the leaving group ends.

Cram discovered a similar phenomenon [81] in studying the

stereochemistry of the deuteroexchange reaction



of the following two substances in the presence of potassium *tert*-butylate:

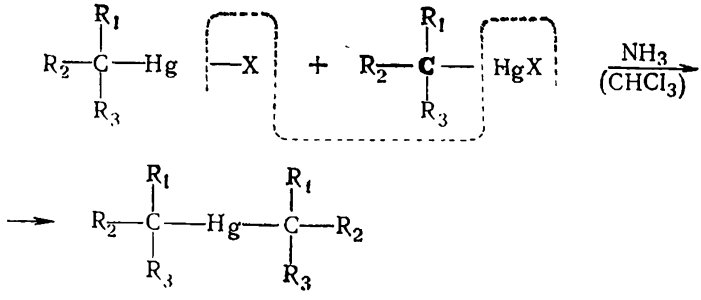


In $(CH_3)_3COD$ as the solvent the exchange of the hydrogen atoms linked with the asymmetric carbon for deuterium both in substance I and in substance II took place with predominant retention of configuration (retention 87-89%). In a mixture of dimethylsulphoxide and $(CH_3)_3COD$ the reaction took place with complete racemization in both cases.

It should be noted that to prove the mechanism of the reactions studied by Cram the results of kinetic investigations are essential.

**Electrophilic Substitution Reactions in Organometallic Compounds.** The greatest progress in the study of the mechanism of electrophilic substitution at the saturated carbon atom was made recently by investigating this reaction in organometallic compounds [60, 82]. This is due largely to the fact that the metal-carbon bond is polarized in a manner favouring $S_E$ reactions. Of all organometallic compounds, organomercury compounds are the most convenient to work with; they are stable under ordinary conditions, but sufficiently reactive, and are readily prepared and identified.

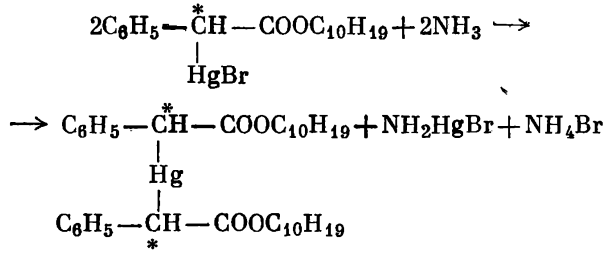
In 1953 the stereochemistry of electrophilic substitution, comprising symmetrization of organomercury salts under the influence of ammonia [83, 84] was established*:



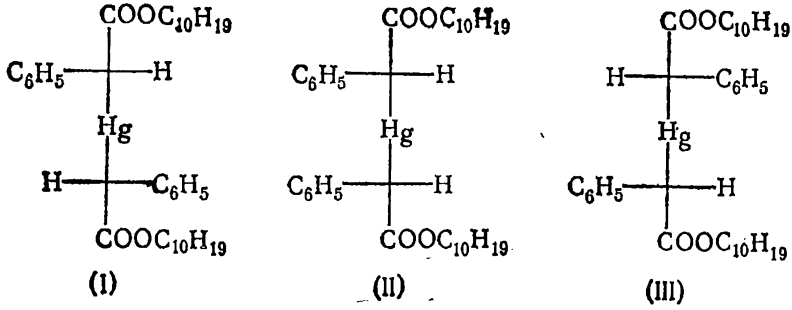
* The carbon atom at which the electrophilic substitution occurs is indicated in bold type.

The initial organomercury compounds were the diastereomeric *l*-menthyl esters of α-bromomercuricphenylacetic acid, in which mercury is linked with the asymmetric carbon atom.

In the symmetrization of one of the diastereomeric *l*-menthyl esters of α-bromomercuricphenylacetic acid:



formation of the following isomers of the symmetrical α-mercurated menthyl ester of phenylacetic acid is formally possible:



(I) (II) (III)

1. If symmetrization takes place with retention of configuration at the asymmetric carbon atoms in both molecules of the initial substance, only one isomer of the end symmetrical organomercury compound (I or III, depending on the configuration of the initial substance) can form.

2. If symmetrization proceeds with retention of configuration of one molecule of the initial substance and racemization of the second molecule, the formation of two isomers is possible, I and II or II and III, depending on the initial substance.

3. If symmetrization takes place with retention of configuration of one molecule of the initial substance and inversion of the second molecule, only isomer II can form irrespective of the configuration of the initial substance.*

---

* Since symmetrization affects the asymmetric carbon atom of only one of the two reacting molecules, the other three formally possible variants (taking into account the case where asymmetric carbon atoms of both reacting molecules are affected) are not considered.

When the *l*-menthyl ester of α-bromomercuricphenylacetic acid with $[\alpha]_D^{18}$—95° (diastereomer I) is symmetrized, a single isomer of the symmetrical organomercury compound is formed with $[\alpha]_D^{18}$—21.4°. If the *l*-menthyl ester of α-bromomercuricphenylacetic acid with $[\alpha]_D^{18}$—49.3° (diastereomer II) is symmetrized, another (also single) symmetrical organomercury compound with $[\alpha]_D^{18}$—7.7° is formed.

These results show that symmetrization takes place with retention of configuration at the asymmetric carbon atoms of both molecules of the initial substance (1st variant).

Another confirmation of this conclusion are the results of the reaction of both symmetrical diastereomers with hydrogen bromide [87, 88]. If the symmetrical compound having $[\alpha]_D^{18}$—2° is reacted with an equimolar quantity of alcoholic hydrogen bromide, the result is an *l*-menthyl ester of α-bromomercuricphenylacetic acid with $[\alpha]_D^{18}$—86°. In the reaction of the symmetrical compound having $[\alpha]_D^{18}$—8° with an equimolar quantity of hydrogen bromide an *l*-menthyl ester of α-bromomercuricphenylacetic acid with $[\alpha]_D^{18}$—49° is formed.

$$\underset{[\alpha]_D^{18}-2^\circ}{R_1R_2R_3C-Hg-CR_1R_2R_3} \xrightarrow{HBr} \underset{[\alpha]_D^{18}-86^\circ}{R_1R_2R_3C-Hg-Br}$$

$$\underset{[\alpha]_D^{18}-8^\circ}{R_1R_2R_3C-Hg-CR_1R_2R_3} \xrightarrow{HBr} \underset{[\alpha]_D^{18}-49^\circ}{R_1R_2R_3C-Hg-Br}$$

### Kinetics of Electrophilic Substitution

A study of the kinetics of symmetrization of organomercury salts by the action of ammonia revealed that the reaction is reversible (goes to completion only with a definite large excess of ammonia) and is of second order with respect to the organomercury salt and of second order with respect to ammonia [89]. Hence, this reaction has a two-stage mechanism. The first stage comprises a bimolecular electrophilic substitution; the second is the binding of the mercuric halide with ammonia:

$$\text{(a)}\quad R_1R_2R_3C-HgX+NH_3 \underset{\longleftarrow}{\overset{\text{Fast}}{\longrightarrow}} R_1R_2R_3C-HgX\cdot NH_3$$

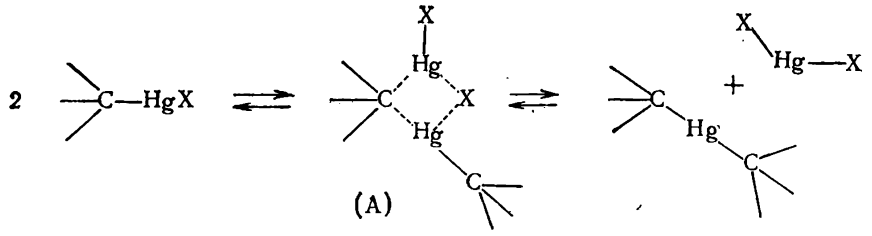
$$\text{(b)}\quad 2R_1R_2R_3C-HgX\cdot NH_3 \xrightarrow{\text{Slow}} (R_1R_2R_3C)_2Hg+HgX_2\cdot(NH_3)_2\,(S_E2)$$

**$S_E2$ Rule and Mechanism of $S_E2$ Reactions.** Thus the same compounds (esters of α-bromomercuricphenylacetic acid) served simultaneously for the study of stereochemistry and of the reaction kinetics of electrophilic substitution at the saturated carbon atom.

As a result of this work a rule was formulated which was confirmed later on other examples: *bimolecular electrophilic substitution*

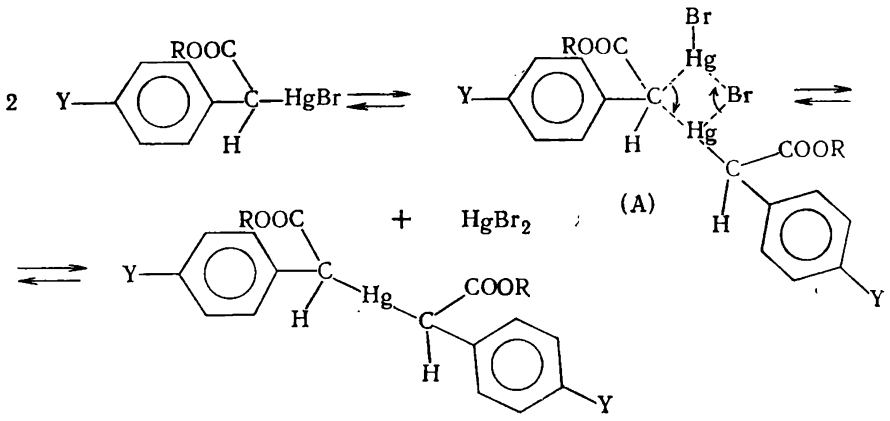
*at the saturated carbon atom takes place with retention of stereochemical configuration* [88, 89].

Taking into consideration stereochemistry and kinetics, the mechanism of the above reactions may be represented by the following scheme*:




As the reactions in question are bimolecular, proceed with retention of configuration and are carried out in nonpolar solvents (without the participation of free ions), it may be concluded that the activated complex (A) in these reactions apparently is cyclic (four-membered) in form**. For this reason these $S_E2$ reactions must be considered $S_Ei$ reactions.

**Effect of Structural Factors.** The effect of polar factors on the rate of reaction was studied extensively on the example of symmetrization (under the action of ammonia) of esters of α-bromomercuricphenylacetic acid having different substituents (Y) in the benzene ring [90, 91]




* Here and in the following when discussing the characteristic features of the symmetrization reaction, for better vividness we shall, as hitherto, examine a four-membered cyclic transition state (A) in the "pure form," so to say, keeping in mind, of course, that in reality either one or both Hg atoms are coordinated with ammonia molecules.

** See however [92, 93].

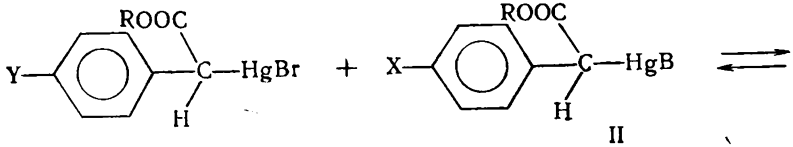
The nature of the substituent Y has an important influence on the rate of symmetrization as it is shown by the values of the corresponding reaction rates:

| Y | $NO_2$ | I | Br | Cl | F | H | $(CH_3)_2CH$ | $CH_3$ | $(CH_3)_3C$ |
|---|---|---|---|---|---|---|---|---|---|
| $K_2 \frac{ml}{mole \cdot sec}$ | — | 670 | 540 | 470 | 148 | 110 | 42 | 34 | 28 |

The results obtained obey Hammett's equation. When $Y = NO_2$, the reaction is too fast for its kinetics to be measured.

Since the effect of the substituents Y on the rate of this reaction is apparently due to purely polar factors (without the participation of steric factors), it follows from the available data that pulling of electrons away from the reaction centre (saturated carbon atom) facilitates the bimolecular reaction of electrophilic substitution ($S_E2$)*. This fact means that even in bimolecular substitution the rupture of the old bond may be more important than the formation of the new one.

As both the old C — Hg and Hg — Br bonds are broken when the transition state (A) is reached, the symmetrization reaction should be expected to proceed faster when unlike molecules of organomercury compounds containing different para-substituents in the benzene rings react with each other. If, for example, Y = electron acceptor, and X = electron-donor substituent, the transition state (A) should be attained more easily than when like molecules react.

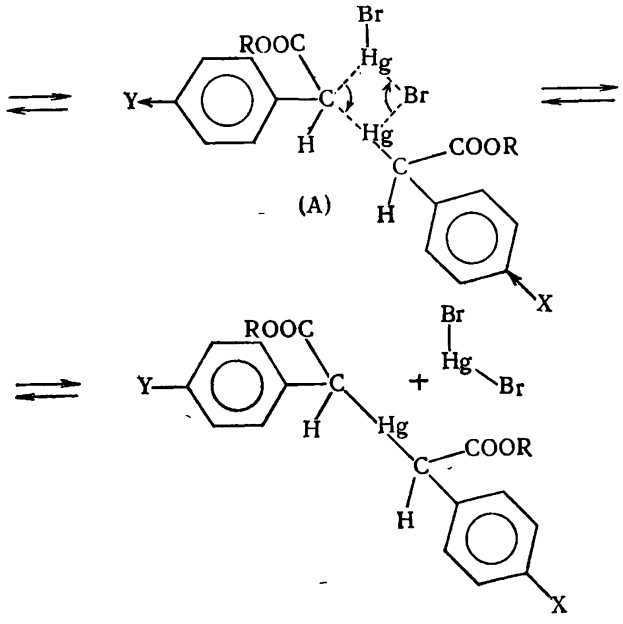



I II

* Naturally, in the case of bimolecular nucleophilic substitution in analogous systems a reverse dependence is observed if the effects of different substituents on the reaction rate are compared. For instance, in the reaction of isotopic exchange

$$p\text{-}YC_6H_4—CH_2—Cl + Li\overset{*}{Cl} \rightleftharpoons p\text{-}YC_6H_4—CH_2—\overset{*}{Cl} + LiCl$$

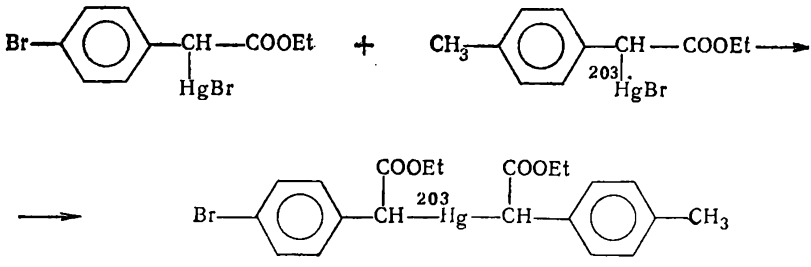
which is a second-order reaction, the value of $K_2 \times 10^5$ for benzyl chloride (Y = H) is 0.243, and for the *p*-methyl substituent ($Y = CH_3$) the value is 2.32 or almost 10 times as large [94].

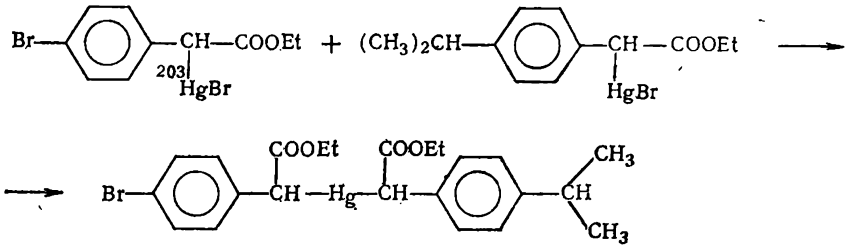



In the first of the reacting molecules rupture of the old C — Hg bond is facilitated, in the second—rupture of the Hg — Br bond.

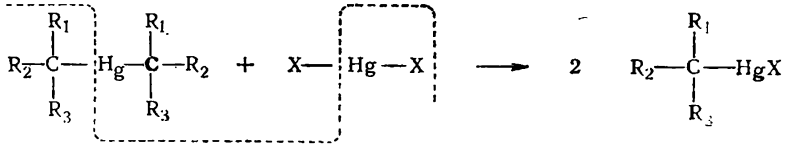
"Cosymmetrization" of this type was carried out with Y and X chosen as H and Cl, H and Br, $CH_3$ and H, respectively [82]. The initial rate of reaction was calculated. In all cases the overall rate of the process was greater than the rate of symmetrization of any of the individual substances in the same concentration.

The fact that the mercury atom which formerly belonged predominantly to the initial organomercury salt with the electron-donor substituent X became part of the symmetrical compound formed, may serve as a confirmation of a cyclic transition state of type (A) in the "cosymmetrization" reaction [82a]:

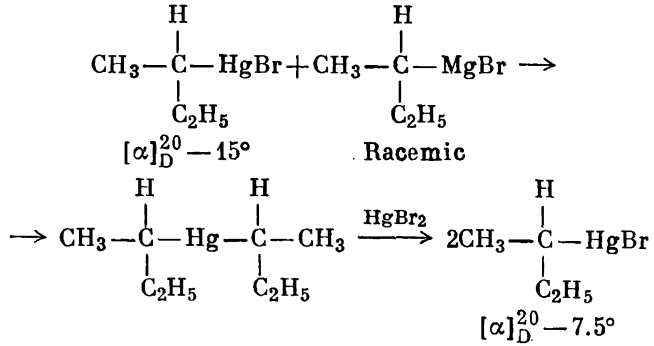




**Reaction of Symmetrical Organomercury Compounds with Mercuric Halide.** The reaction of symmetrical organomercury compounds of the type $(R_1R_2R_3C)_2Hg$ with mercuric halide may serve as another example of electrophilic substitution at the saturated carbon atom:



The simplest case of such a reaction was studied by Charman, Hughes and Ingold [92] and almost simultaneously by Jensen and coworkers [95]. These workers converted optically active *sec*-butylmercuric bromide into the symmetrical di-*sec*-butylmercury by the action of racemic *sec*-butylmagnesium bromide. Then they treated the symmetrical compound obtained with mercuric bromide and again *sec*-butylmercuric bromide resulted, but its optical activity was now only half of what it had been formerly:



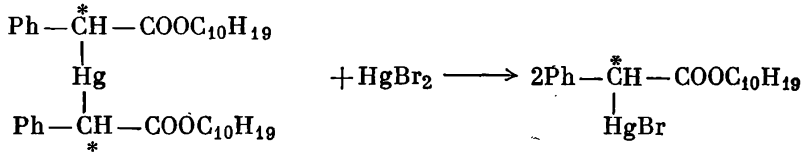
It follows from these results that the reaction of di-*sec*-butylmercury with mercuric bromide proceeds with retention of configuration*.

Further, a study of the kinetics of the reaction revealed that it is first-order with respect to di-*sec*-butylmercury and first-order

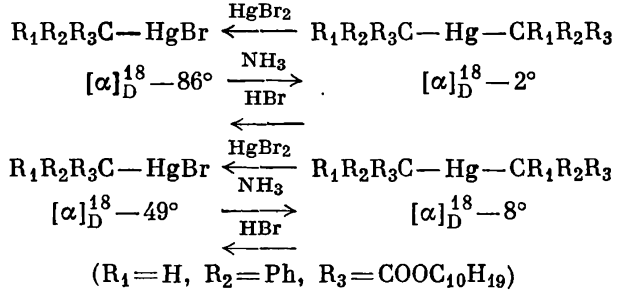
* Retention of configuration was also found when a similar cycle of reactions were carried out with optically active 5-bromomercuric-2-methylhexane [96].

with regard to mercuric bromide. This confirmed the rule stating that reactions of bimolecular electrophilic substitution at the saturated carbon atom proceed with retention of configuration.

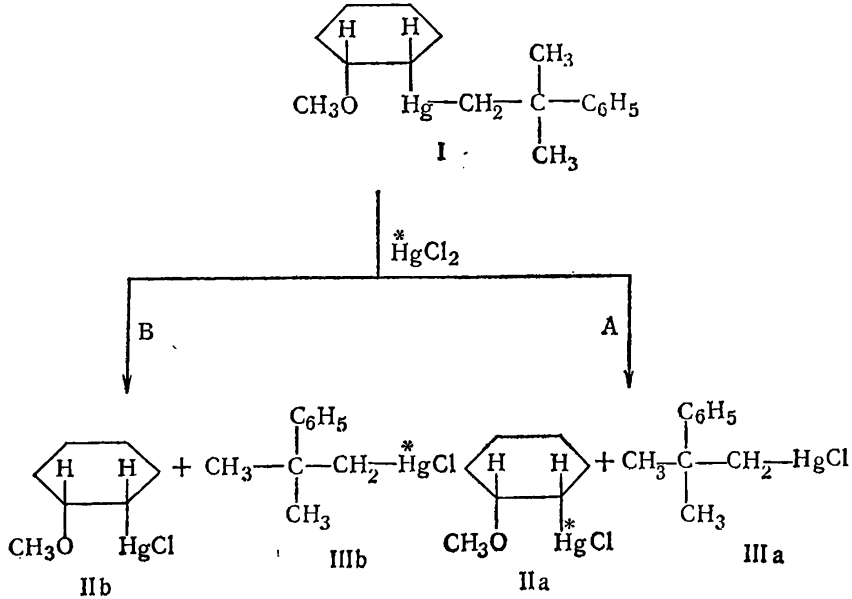
The stereochemistry of reactions of symmetrical organomercury compounds with mercuric halide were also studied with the diastereomeric symmetrical α-mercurated *l*-menthyl esters of phenylacetic acid [87]:



In both cases retention of configuration was found. Thus, the stereochemical relations in symmetrization reactions and reverse reactions of the same may be depicted by the following schemes [87, 88]:



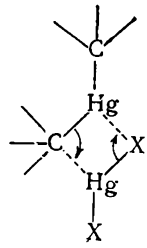
Winstein, Traylor and Garner [114] investigated the reaction



of *cis*-2-methoxycyclohexylneophenylmercury I in ether solution at —5° with $HgX_2$ containing radioactive mercury $Hg^{203}$ [97].

Of the two directions (A and B) the first is an $S_E$ reaction at the asymmetric carbon atom of the six-membered ring. This reaction also proceeds with retention of configuration.

For the $S_E2$ reactions of symmetrical organomercury compounds with mercuric chloride the following four-membered cyclic transition state (A) was proposed [60, 88]:




(A)

The data [119], on the basis of which a more complex transition state was proposed, could not be confirmed [120].

### Electrophilic Isotope Exchange Reactions of Organometallic Compounds

Several types of isotope exchange reactions in organomercury compounds have been discovered and investigated recently. These are reactions of electrophilic substitution at the saturated carbon atom:

(a) $R_1R_2R_3C-HgX+H\overset{*}{g}X_2 \rightleftarrows R_1R_2R_3C-H\overset{*}{g}X+HgX_2$

(b) $R_1R_2R_3C-HgX+R_4R_5R_6C-H\overset{*}{g}X \rightleftarrows R_1R_2R_3C-H\overset{*}{g}X+R_4R_5R_6C-HgX$

(c) $R_1R_2R_3C-Hg-CR_1R_2R_3+R_1R_2R_3C-H\overset{*}{g}X \rightleftarrows$

$\rightleftarrows R_1R_2R_3C-H\overset{*}{g}-CR_1R_2R_3+R_1R_2R_3C-HgX$

**Bimolecular Electrophilic Substitution ($S_E2$).** Isotope exchange reactions of organomercuric salts with a mercuric halide may serve as examples of the simplest reactions of electrophilic substitution at the saturated carbon atom:

$$RR'R''C-\vdots HgX+X-\vdots \overset{*}{H}gX \rightleftarrows RR'R''C-H\overset{*}{g}X+HgX_2$$

Kinetic studies of these reactions on the examples of alkylmercuric bromides [98], esters of α-bromomercuricphenylacetic acid [60, 99] and other mercuriated carbonyl compounds [100] as well as ben-

zylmercuric chloride [101] have shown that in the majority of cases these reactions follow the $S_E2$ mechanism.

In a study of isotope exchange between alkylmercuric bromides and mercuric bromide [98] the reaction as a whole was found to be second-order (the order with respect to each component not having been determined). On the basis of these results the following general mechanism of isotope exchange covering the above types was proposed:

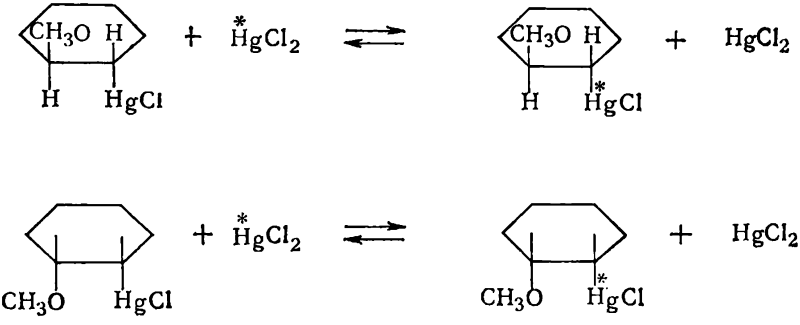
$$\text{(a)}\quad 2RR'R''C{-}HgX \rightleftharpoons (RR'R''C)_2Hg + HgX_2$$

$$\text{(b)}\quad (RR'R''C)_2Hg + \overset{*}{H}gX_2 \rightleftharpoons RR'R''C{-}\overset{*}{H}gX + RR'R''C{-}HgX$$

Probably such a mechanism is possible in principle. However, as the order with respect to each of the components of the reaction was not determined, it is impossible to make a choice between this two-stage mechanism [$S_E2$ being stage (*a*)] and the mechanism of simple bimolecular substitution, in which the order with respect to each component should be unity.

In those cases where the order of each component was determined [100, 101], it was found to equal unity with respect to both the organomercury salt and the mercuric halide; thus, in these cases the two-stage mechanism was erroneous.

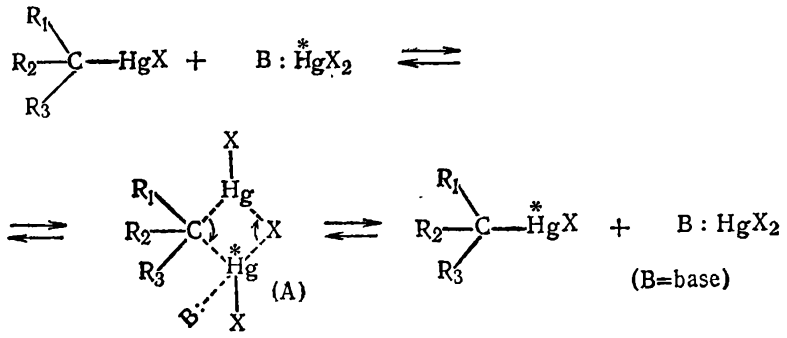
The stereochemistry of the isotope exchange reaction under consideration was studied for the reaction between *cis*- and *trans*-2-methoxycyclohexylmercuric chloride. It was found that both isomers react with mercuric chloride, labeled with $Hg^{203}$, with retention of geometric configuration [102]:



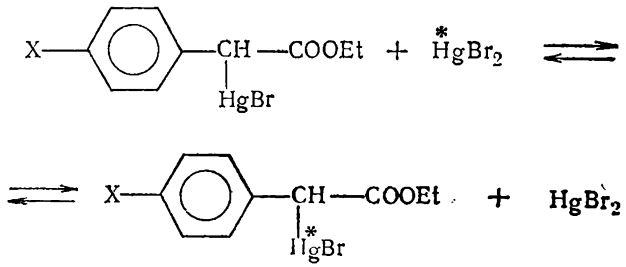

Isotope exchange reactions of this type are accelerated by bases, for example, by pyridine or quinoline.

Taking into consideration kinetics and stereochemistry, the $S_E2$ reaction mechanism of isotope exchange of organomercuric salts

with mercuric halide may be represented by the following scheme*:

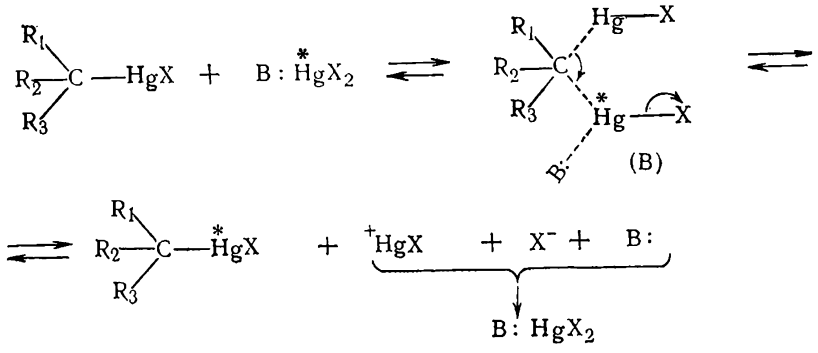



**Monomolecular Electrophilic Substitution.** It must be remembered that the mechanism of the reaction in question may change when the reaction medium is changed. This was first proved [103] for the following example:



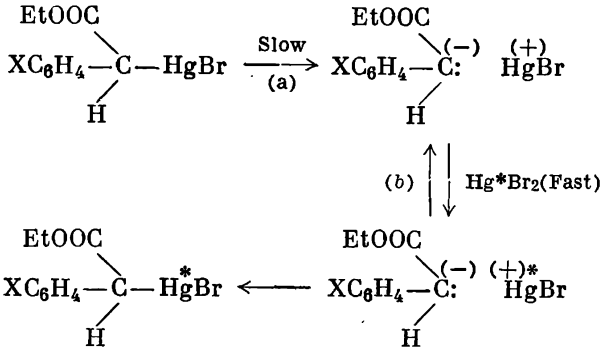
In pyridine this reaction is of overall second-order (first-order with respect to each of its components). In this case, like in all

* The cyclic transition state shown in this scheme is the more probable in reactions of this type, the less polar the solvent. In polar solvents, for instance, in pyridine, the possibility of an acyclic transition state of type (B) cannot be excluded:



those previously described, this is a bimolecular reaction of electrophilic substitution ($S_E2$).

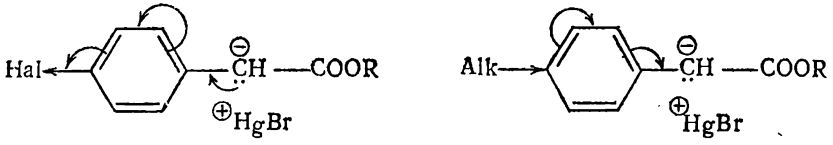
When 70% aqueous dioxane is used as the reaction medium, the kinetics of the reaction changes. It is first-order with respect to the ethyl ester of α-bromomercuricarylacetic acid and zero-order with respect to mercuric bromide. The change in kinetics is indicative of the change in the reaction mechanism. Evidently, under these conditions the first slow stage of the reaction consists of ionization with the formation of an ionic pair*:




In the order of increasing accelerating effect on the reaction the substituents X form the series:

$$I, Br, Cl > F > H > CH_3 > (CH_3)_3C$$

Such a dependence of the reaction rate on the nature of the substituent is in full agreement with the $S_E1$ mechanism. Electronegative substituents, which pull electrons away, should facilitate the formation of an ionic pair and thus accelerate the reaction. The effect of electropositive substituents should be such as to increase the electron density at the α-carbon and to impede ionization of the C — Hg bond:




* The concept of ionic pairs was developed by Winstein [104]. According to this concept the anion and cation formed under definite conditions as a result of ionization are not independent of each other, but form a unified whole—an ionic pair, which is more reactive than the initial compound. Naturally, in these cases ionization should be distinguished from dissociation because dissociation results in free ions (though generally solvated).

The effect of substituents on an $S_E2$ reaction is generally different. For example, in the case of the $S_E2$ reaction of isotope exchange of the type [101]

the substituents X fall into the following series in order of accelerating effect on the reaction:

$$(CH_3)_2CH > CH_3 > H > Cl > F$$

The above isotope exchange reaction of the ethyl ester of α-bromomercuricphenylacetic acid proceeds readily according to an $S_E1$ mechanism in dimethyl sulphoxide which possesses high ionizing power.

The rate of the isotope exchange reaction of organomercury salts with mercuric halide rises with increasing basic properties of the solvent. As it was shown for the example of reactions in dimethyl formamide [105], such an increase in reaction rate is at least partly due to the participation in the reaction of complexes of mercuric chloride with a base rather than the low-polar molecules of mercuric halide, the former being more electrophilic than mercuric halide.

An example is known where a reaction of isotope exchange between molecules of different organomercuric salts [106] was carried out in pyridine at 60°. This reaction is first-order with respect to each of the components and it evidently proceeds according to the $S_E2$ mechanism:

$$R_1R_2R_3C-HgBr + Ph-Hg^*-Br \rightleftharpoons R_1R_2R_3C-Hg^*Br + Ph-Hg-Br$$
$$(R_1=H,\ R_2=Ph,\ R_3=COOEt)$$

Stereochemical and kinetic investigation of the reaction

$$R_1R_2R_3C-Hg-CR_1R_2R_3 + R_1R_2R_3C-Hg^*Br \rightleftharpoons$$
$$\rightleftharpoons R_1R_2R_3C-Hg^*-CR_1R_2R_3 + R_1R_2R_3C-HgBr$$
$$[R_1=H,\ R_2=CH_3,\ R_3=(CH_3)_2CHCH_2CH_2]$$

showed that its elementary act consists in exchange of the Br atom in the molecule of the organomercuric salt for the $R_1R_2R_3C$ group from the symmetrical organomercury compound molecule [107].

The groups are transferred from one mercury atom to another with strict retention of configuration*:

$$R_1R_2R_3C-Hg\,|\,-CR_1R_2R_3 + R_1R_2R_3\overset{*}{C}-\overset{203}{Hg}\,|\,-Br \rightleftharpoons$$

$$\rightleftharpoons R_1R_2R_3C-Hg\,|\,-Br + R_1R_2R_3\overset{*}{C}-\overset{203}{Hg}-CR_1R_2R_3 \rightleftharpoons$$

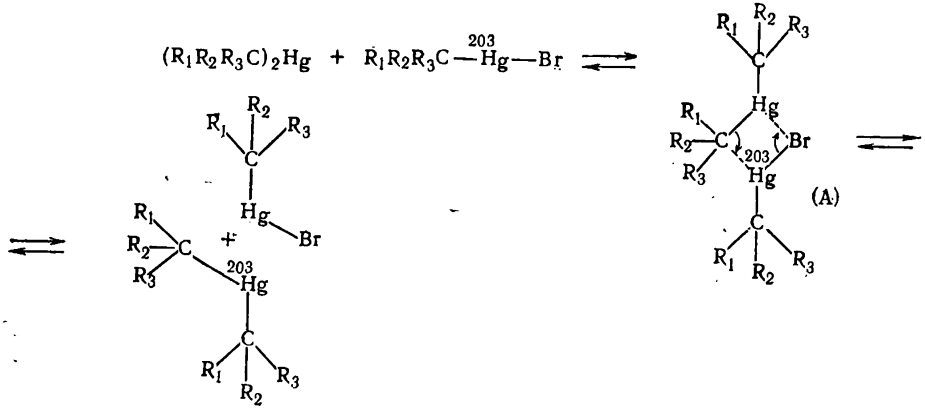
$$\rightleftharpoons R_1R_2R_3C-Hg-\overset{*}{C}R_1R_2R_3 + Br-\overset{203}{Hg}-CR_1R_2R_3 \text{ etc.}$$

The relationship between the degree of isotope exchange ($F$) and the degree of group distribution ($F'$) may be expressed by the following equation:

$$\ln(1-F') = \frac{2A+B}{2(A+B)}\ln(1-F)$$

($A$ = concentration of $R_1R_2R_3C - Hg - CR_1R_2R_3$, $B$ = concentration of $R_1R_2R_3C - Hg - Br$).

The transition state of this reaction, evidently, has the form of the usual four-member cycle (A):



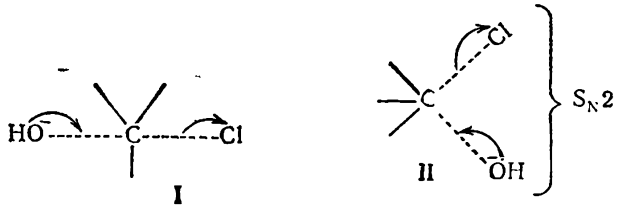

Using the above equation it is possible to calculate the degree of isotope exchange ($F$) at any given instant of the reaction from the experimentally determined degree of redistribution of groups ($F'$); and conversely, knowing the degree of isotope exchange, the degree of redistribution of groups can be calculated.

The excellent agreement between calculated and experimentally determined values indicates that *each elementary step of the reaction of bimolecular electrophilic substitution takes place with retention of stereochemical configuration.*

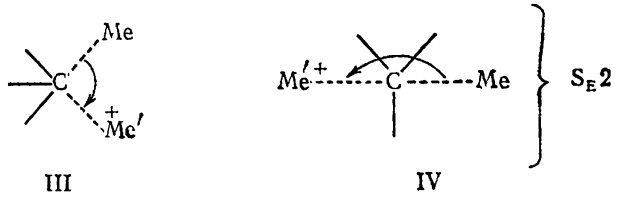
* A similar investigation (using *sec*-butyl organomercury compounds) was published somewhat later by Ingold and coworkers [93].

**The Limits of Applicability of the $S_E2$ Rule and the $S_E1$ Rule.** Before leaving the subject of the mechanism of bimolecular reactions of electrophilic substitution at the saturated carbon atom, it is important to find the answer to the following natural question: Is the $S_E2$ rule, derived from investigations of the reactivity of organomercuric compounds alone, general?

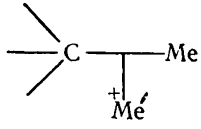
As is known, inversion of configuration in $S_N2$ reactions at the saturated carbon atom is due to the fact that of the two possible transition states, (I) and (II), the first is energetically more advantageous:




Similarly of the two possible transition states (III) and (IV) in $S_E2$ reactions the state (III) must be energetically preferable (not to mention stabilization due to the formation of a four-membered ring which is often possible)




Drawing an analogy with π complexes it might be expected that the transition state (III) arises from the preliminarily formed σ complex (V):




V

However, contrary to π complexes, there is no experimental proof so far of the existence of such σ complexes; on the other hand, it is difficult to object to the assumption that formation of the transition state (III) is preceded by an attack by a cation $Me'^{+}$ on

the C — Me bond, so to speak in the hypothetical sense, of the σ complex (V).

As to the steric factors, they are not very favourable for retention of configuration in the case of organomercuric compounds because of the large covalent and van der Waals radius of the mercury atom. Thus, the steric factor hindering attainment of the transition state (III) cannot change the stereochemical result of the reaction even in the case of very large Me and Me′.

It follows from the above discussion that the rule of retention of configuration in $S_E2$ reactions should be fairly general in nature.

Although kinetic investigations are needed for formulation of the $S_E1$ rule, it can be assumed, on the basis of Cram's work [73-81] that $S_E1$ reactions should proceed with racemization, accompanied by partial inversion of configuration increasing with growing concentration (and strength) of the electrophilic reagent reacting with the molecule in question.

**Electrophilic Substitution of Halogen for Mercury.** Jensen [95] studied the stereochemistry of the reaction of organomercuric compounds with bromine.

The reaction between optically active 2-bromomercuricbutane and bromine in pyridine at —40° and —65° results in optically active 2-bromobutane:

$$\underset{\substack{|\\ HgBr\\ [\alpha]_D^{22}-28.5^\circ}}{CH_3-CH}-CH_2-CH_3+Br-Br \xrightarrow{C_5H_5N} \underset{\substack{|\\ Br\\ [\alpha]_D^{22}-6.3^\circ}}{CH_3-CH}-CH_2-CH_3+HgBr_2$$

It is most probable that this reaction proceeds with retention of stereochemical configuration and is a reaction of electrophilic substitution at the asymmetric carbon atom.

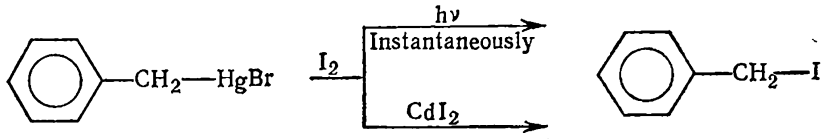
This conclusion is borne out by the fact that in nonpolar solvents, say, in carbon bisulphide, i.e., under conditions favouring radical reactions, the exchange of mercury for bromine involves racemization, inactive 2-bromobutane being formed.

In all the cases described, where the kinetics of an electrophilic reaction of substitution of a halogen for mercury was investigated [108], the latter reaction was bimolecular ($S_E2$).

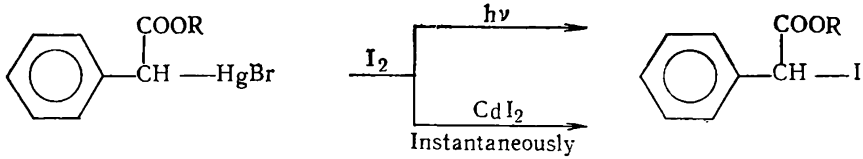
The rates of electrophilic and radical reactions of halogens with organomercury compounds depend essentially on the structure of the latter [109].

Thus, the radical (photochemical) reaction between benzylmercuric bromide and iodine in carbon tetrachloride takes place instantaneously, but the heterolytic reaction in the presence of cadmium iodide proceeds at a measurable rate (the reaction is

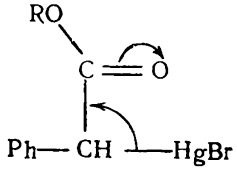
first-order with respect to each of the components).




Conversely, esters of bromomercuricphenylacetic acid react instantaneously with iodine heterolytically (in the presence of cadmium iodide) and quite slowly—radically (first-order with respect to iodine, zero-order with respect to the organomercuric salt).




The faster rate of the electrophilic reaction in this case, compared to benzylmercuric bromide, is apparently due to the fact that conjugation of the mercury-carbon bond with the carbonyl group facilitates heterolytic rupture of this bond




**Electrophilic Exchange of Mercury for Hydrogen.** Fully substituted organomercury compounds react readily with mineral or carboxylic acids to form organomercury salts

$$R—Hg—R+H—X \longrightarrow R—Hg—X+R—H$$

The organomercury salts are more stable, being decomposed only by mineral acids:

$$R—HgX+H—X \longrightarrow R—H+HgX_2$$

The stereochemistry of reactions of this type has not been studied, but a number of papers on their kinetics have been published [110-117].

The reaction of unsymmetrical fully substituted organomercury compounds with hydrochloric acid was used by Kharasch [118]

to establish an electronegativity series of organic groups:

$$R-Hg|-R'+H-Cl \longrightarrow R-Hg-Cl+H-R'$$

(R′ is more electronegative than R)

Below is given Kharasch's series in which groups are arranged in the order of diminishing electronegativity:

$$CN > p\text{-}C_6H_4OCH_3 > o\text{-}C_6H_4OCH_3 > \alpha\text{-}C_{10}H_7 > o\text{-}C_6H_4CH_3 >$$
$$> p\text{-}C_6H_4CH_3 > m\text{-}C_6H_4CH_3 > C_6H_5 > p\text{-}C_6H_4Cl > o\text{-}C_6H_4Cl >$$
$$> m\text{-}C_6H_4Cl > CH_3 > C_2H_5 > C_3H_7 > C_4H_9 > C_6H_5CH_2 > (CH_3)_3C$$

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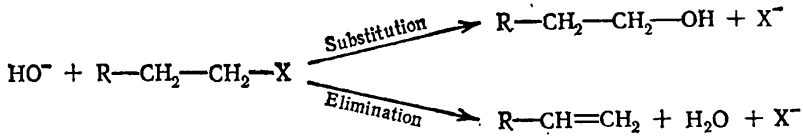
# 3

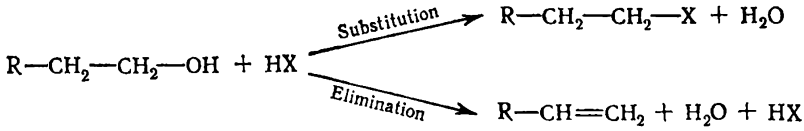
## ELIMINATION REACTIONS

### 3-1 GENERAL

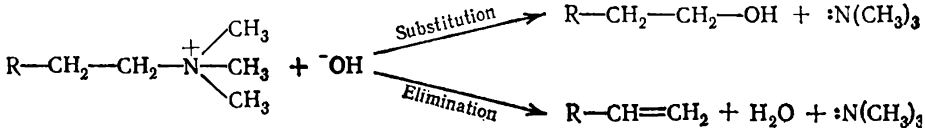
Reactions of nucleophilic substitution at the saturated carbon atom are accompanied in the majority of cases by reactions of elimination resulting in the formation of olefins. Examples are: reactions of alkyl halides with alkalies




the reaction between alcohols and mineral acids



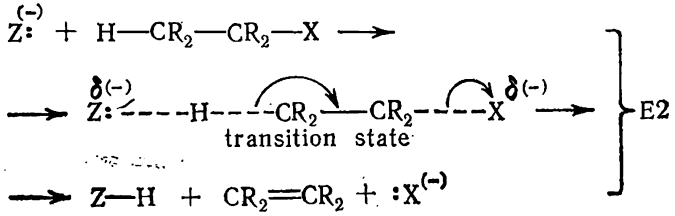

and decomposition of quaternary ammonium bases




In many cases, as, for instance, in the decomposition of quaternary ammonium bases, elimination is the predominant reaction. The fact that elimination reactions take place simultaneously with reactions of nucleophilic substitution indicates that these reactions have a common mechanism. The truth of this supposition has been confirmed by special investigations [1].

## 3-2 BIMOLECULAR MECHANISM*

Bimolecular elimination $E2$ corresponds to bimolecular substitution $S_N2$: the approaching reagent Z of a nucleophilic (partly basic) nature promotes elimination of proton while the electron-acceptor group X simultaneously departs with the previously shared electron pair:




The curved arrows show the transfer of electron pairs which formerly comprised covalent bonds.

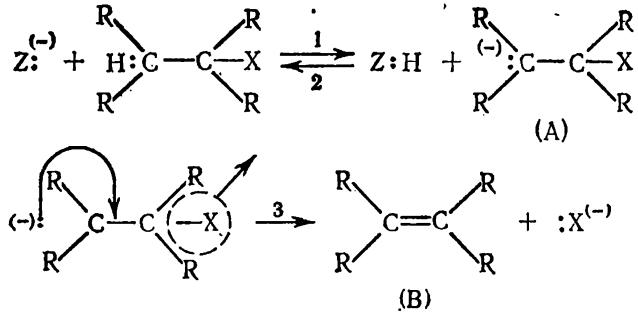
In this reaction reagent Z and the leaving substituent X do not necessarily have to be negative ions, as is evident from the listed meanings of Z and X:

$$Z = H_2O;\ N(CH_3)_3;\ CH_3COO^-;\ O_2NC_6H_4O^-;\ C_6H_5O^-;$$
$$OH^-;\ OC_2H_5^-;\ NH_2^-;\ CO_3^{--};$$
$$X = -\overset{+}{N}R_3;\ -\overset{+}{P}R_3;\ -\overset{+}{S}R_2;\ -SO_2R;\ -Cl;\ -Br;\ -I;\ -OS_2R;\ -OCOR$$

A bimolecular mechanism (designated $E2$) has been proved kinetically for cases where

$$Z = OH^-;\ OC_2H_5^-$$
$$X = -\overset{+}{N}R_3;\ -\overset{+}{S}R_2;\ -Cl;\ -Br;\ -I$$

In elimination reactions of this type, taking place under the influence of basic reagents, the process commences with the attack by the base on the β-hydrogen, resulting in the formation of a transient carbanion (A), followed by the elimination from the latter of group X with the electron pair which previously made the C—X bond, to form an olefin (B):




* See [14].

Actually such a process does not take place in stages (with the formation of carbanion as a kinetically independent particle) but continuously, as was proved experimentally by using the isotope method for studying the reaction (kinetically second-order) of preparation of styrene from β-bromoethylbenzene and sodium ethoxide in $C_2H_5OD$ solution [2].

For this reaction either a one-step or a two-step mechanism may be proposed:

$$C_2H_5O^{(-)} + C_6H_5-CH_2-CH_2Br \longrightarrow C_2H_5-\ddot{O}\cdots H\cdots \underset{\displaystyle C_6H_5}{\underset{|}{CH}}-CH_2\cdots \ddot{Br}: \longrightarrow$$

$$\longrightarrow C_2H_5-OH + C_6H_5-CH=CH_2 + :\ddot{Br}:^{(-)} \qquad \text{(I)}$$

$$\text{(1)}\quad C_2H_5\ddot{O}:^{(-)} + C_6H_5-CH_2-CH_2-Br \underset{(b)}{\overset{(a)}{\rightleftharpoons}}$$

$$\rightleftharpoons C_2H_5OH + C_6H_5-\ddot{C}H^{(-)}-CH_2-Br$$

$$\text{(2)}\quad C_6H_5-\ddot{C}H^{(-)}-CH_2-Br \xrightarrow{(c)} C_6H_5-CH=CH_2 + :\ddot{Br}:^{(-)} \qquad \text{(II)}$$

As step (1) in the two-step mechanism must be reversible, the carbanion formed can react with $C_2H_5OD$*, as a result of which the unreacted β-bromoethylbenzene should contain deuterium:

$$C_2H_5-\ddot{O}:^{(-)} + C_6H_5-CH_2-CH_2-Br \longrightarrow$$

$$\longrightarrow C_2H_5-OH + C_6H_5-\ddot{C}H^{(-)}-CH_2-Br$$

$$\uparrow\downarrow C_2H_5OD$$

$$C_6H_5-\underset{\displaystyle D}{\underset{|}{CH}}-CH_2-Br + C_2H_5-\ddot{O}:^{(-)}$$

But if the reaction follows scheme (I) the unreacted bromoderivative should contain no deuterium.

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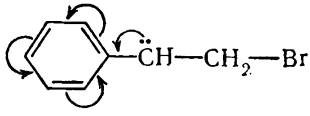
* Such a supposition would have been improbable only if reaction (*c*) took place much faster than reactions (*a*) and (*b*). In the case under consideration, however, this is not so, because the carbanion

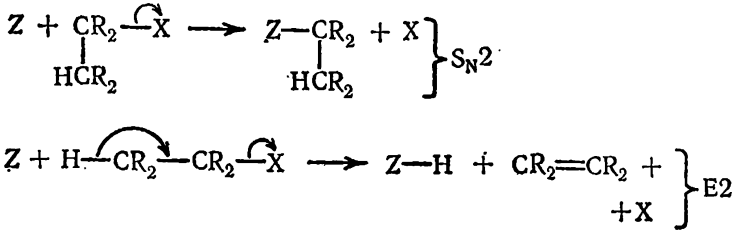


is stabilized to some extent owing to conjugation of the free electron pair with the π electrons of the benzene ring.

Experiment showed that after carrying the elimination of hydrogen bromide to 50%, the unreacted β-bromoethylbenzene contained no deuterium.

Thus the reaction was proved to be single-step *E*2*. Many factors favouring bimolecular substitution $S_N2$ also promote bimolecular elimination.

This can be better understood by drawing a formal analogy between these two processes.

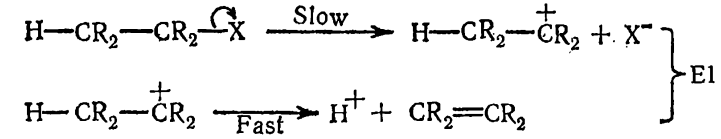


In both cases the electrons are transferred from Z to X; the electrical charges of Z and X are of the same nature and undergo the same changes in the $S_N2$ as in the *E*2 reaction.

### 3-3 MONOMOLECULAR MECHANISM

Elimination reactions are known, which take place irrespective of the concentration of hydroxyl ions or of other basic reagents. Examples of such reactions are the elimination of hydrogen bromide from *tert*-butyl bromide or the elimination of hydrogen chloride from methyldiphenylchloromethane. Such reactions are called *E*1 reactions.

A mechanism analogous to the $S_N1$ mechanism [3] is proposed for them:



As in the case of the $S_N1$ reaction, the main role in this case is played by solvation of the leaving group, for example:

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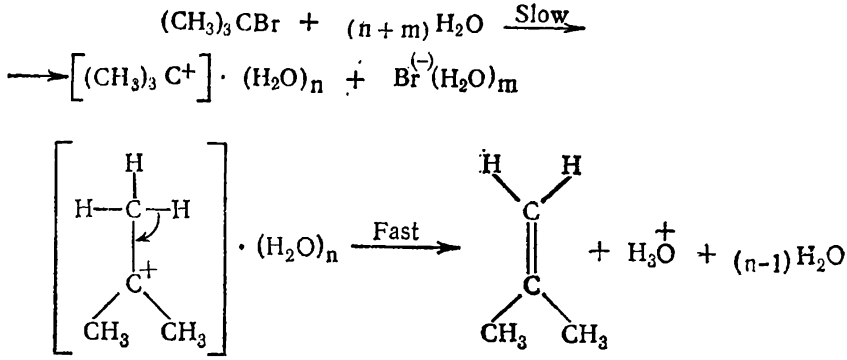
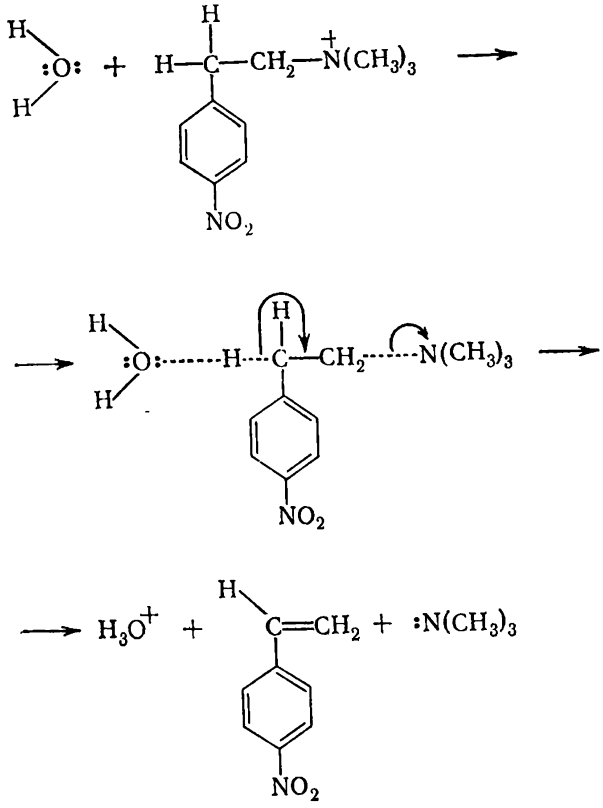
* Since the reaction mechanism becomes monomolecular if the rates of (*a*) and (*b*) are greater as compared with (*c*), *E*2 can be distinguished from *E*1 by using an isotope procedure.



While quaternary ammonium salts, primary and secondary alkyl halides generally react according to $E2$ mechanism, tertiary alkyl halides and sulphonium salts react according to the $E1$ mechanism.

The fact that a reaction is kinetically first-order does not yet provide any proof that it follows an $E1$ mechanism. For instance, decomposition of the quaternary salt dimethyl-β-(*p*-nitrophenyl)-ethylamine in aqueous solution is a first-order reaction. But there is no doubt that this reaction follows an $E2$ mechanism because its rate increases sharply if a nucleophilic reagent stronger than water is added:



Factors favouring nucleophilic substitutions according to $S_N1$ generally promote elimination reactions according to $E1$.

Data proving or disproving that a reaction follows an $E1$ mechanism can be obtained by studying the behaviour of the corresponding reactants in nonaqueous media, and by studying the hydrolysis of alkyl halides containing different halogen atoms.

Optically active α-chloroethylbenzene racemizes in liquid sulphur dioxide solution. The rate of racemization is, in this case, independent of the presence of chloride ions because this racemization is the result of the following reversible reaction:

$$C_6H_5—CHCl—CH_3 \rightleftharpoons C_6H_5—CH=CH_2+HCl$$

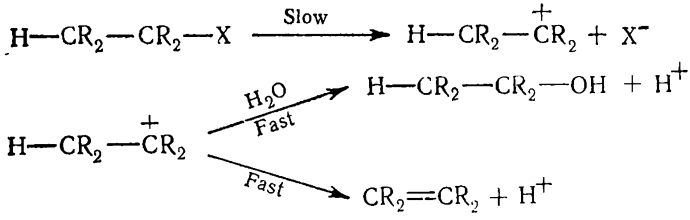
The course of this reaction is borne out by experimental data; thus, if a solution of α-chloroethylbenzene in liquid sulphur dioxide is left standing for a long time at 0°, small amounts of styrene or polystyrenes can be detected in it besides the unchanged original compound. If bromine is added to the α-chloroethylbenzene solution in liquid sulphur dioxide, partial formation of dibromostyrene and chlorobromostyrene occurs. Addition of bromine to a solution of α-bromoethylbenzene in liquid sulphur dioxide results in quantitative formation of dibromostyrene.

α-Chloroethylbenzene racemizes faster in formic acid than in liquid sulphur dioxide. On prolonged standing of a concentrated solution of α-chloroethylbenzene in formic acid, formation of polystyrenes is observed; this process can be accelerated by blowing nitrogen through the solution, as nitrogen sweeps out the hydrogen chloride formed.

*Tert*-butyl chloride reacts similarly in these solvents. In formic acid it produces isobutylene and hydrogen chloride; in the presence of bromine it gives isobutylene dibromide.

The facts cited are in full agreement with the proposed monomolecular nature of the elimination reactions of α-haloethylbenzenes and *tert*-butyl chloride.

In the hydrolysis of alkyl halides possessing different halogen atoms, according to the monomolecular mechanism, the probable direction of the reaction (substitution or elimination) is independent of the nature of the anion X but depends on the nature of the group R:



The rate of ionization $K_{ion}$ determines the overall rate of the process $K_1$. Thus $K_{ion} = K_1 = K_{S_N1} + K_{E1}$ ($K_{S_N1}$ being the substitution rate constant and $K_{E1}$, the elimination rate constant). The ratio $\frac{K_{E1}}{K_1}$ should depend only on the nature of the group R but not on the nature of the halide.

Data on the hydrolysis of *tert*-butyl and *tert*-amyl derivatives are given in Table 3-1.

TABLE 3-1

| Halogen | *Tert*-butyl | | *Tert*-amyl | |
|---|---|---|---|---|
| | $10^5K_1$ | $K_{E1}/K_1$ | $10^5K_1$ | $K_{E1}/K_1$ |
| Chloride | 0.854 | 0.168 | 1.50 | 0.333 |
| Bromide | 37.2 | 0.126 | 58.3 | 0.262 |
| Iodide . . . | 90.1 | 0.129 | 174 | 0.260 |

On passing from chloride to bromide and then to iodide, the overall rate of reaction increases 30-130 times while the ratio $K_{E1}/K_1$ remains more or less constant. These data also support the hypothesis that the direction of the reaction is determined after the alkyl group separates from the halogen atom.

The ratio between the substitution and elimination reactions, whether they proceed according to the monomolecular or bimolecular mechanism, is influenced by a number of factors (concentration of the base, basic properties of the reagent, polarity of the solvent).

## 3-4 FACTORS INFLUENCING RATIO BETWEEN SUBSTITUTION AND ELIMINATION REACTIONS

**Concentration of the Base.** Since the rates of the $E1$ and $S_N1$ reactions are independent of the base, lowering the concentration of the latter will make these reactions predominant, because the rate of second-order reactions ($E2$ and $S_N2$) is lowered with decreasing concentration of the base.

In first-order reactions, if it is assumed that the carbonium ion decomposes partly before colliding with the reagent anion, the ratio of the rate of elimination to the rate of reaction *in toto* ($E1/E1 + S_N1$) must depend on the structure of the carbonium ion and be independent of the concentration of the base. This is borne out by experiment.

As the concentration of alkali increases, second-order reactions begin to predominate. The percentage of olefin formed is nearly constant because the proportion of reaction products depends on the ratio of the corresponding rates of formation.

As the equation below shows, this ratio remains constant for second-order reactions:

$$\frac{\text{Amount of olefin}}{\text{Amount of olefin and amount of substitution product}} = \frac{\text{Rate of formation of olefin}}{\text{Rate of formation of olefin and rate of substitution}} =$$

$$= \frac{K_E[\mathrm{RX}][\mathrm{OH}]}{K_E[\mathrm{RX}][\mathrm{OH}] + K_S[\mathrm{RX}][\mathrm{OH}]} = \frac{K_E}{K_E + K_S} = K$$

($K_E$ = elimination rate constant; $K_S$ = substitution rate constant).

It follows that a change in concentration of the basic reagent may shift the reaction mechanism either towards $E1—S_N1$ or towards

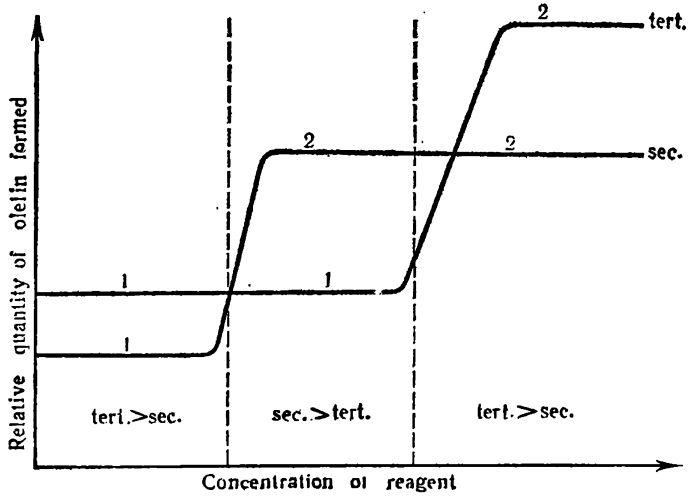



FIGURE 3-1 Dependence of relative quantity of olefin formed on concentration of strong nucleophilic reagent (Numbers on the curves indicate the kinetic order of reaction; *tert.*—tertiary alkyl halide, *sec.*—secondary alkyl halide.)

$E2—S_N2$, but within the limits of the same kinetic order the ratio of the reaction products is independent of the concentration of reagent.

The relation between the relative amount of olefin formed and the concentration of the strong nucleophilic reagent is shown in Fig. 3-1.

The quantitative correlations given in Fig. 3-1 are presented in Table 3-2.

TABLE 3-2

**Amount of Olefin Formed From Isopropyl Bromide and *Tert*-Butyl Bromide in Neutral and Basic Solution at 55°**

| [$C_2H_5ONa$] | None | 0.05 *N* | 2.00 *N* |
|---|---|---|---|
| Kinetic order . . . . | First | Mixed | Second |
| Isopropyl : olefin . . | ~ 3% | 71% | 79% |
| *Tert*-butyl : olefin . . | 27% | 34% | 93% |

**Basic Properties of Reagent.** As was shown in the preceding section, an increase in concentration of the nucleophilic reagent promotes a change from monomolecular to bimolecular mechanism in both substitution and elimination reactions. A similar change in mechanism is observed when weak nucleophilic reagents are replaced by strong ones. However, as weak electrophilic reagents are replaced by stronger ones the ratio of elimination and substitution reaction rates $K = \frac{K_1E2}{K_2S_N2}$ does not remain constant. This is due to the fact that in elimination reactions the nucleophilic reagent reacts directly with the hydrogen atom while in substitution reactions it reacts with the carbon atom; there is no parallelism in the action of the reagent on C and H atoms.

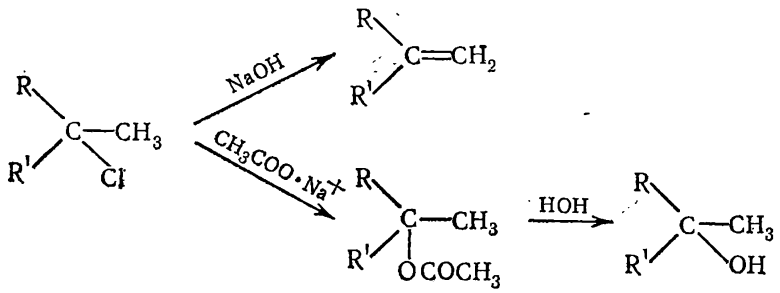
Thus, halide ions practically do not react with hydrogen as nucleophilic reagents but do react with carbon in $S_N2$ reactions; this is confirmed by the racemization of optically active halogen derivatives caused by the action of the corresponding halide anions. If nucleophilic reagents are used in the following sequence:

$$\underset{\text{Weakening of nucleophilic properties}}{\xrightarrow{\text{AlkO}^-\ \text{HO}^-\ \text{C}_6\text{H}_5\text{O}^-\ \text{CH}_3\text{COO}^-\ \text{Br}^-}}$$

the ratio $\frac{K_1E2}{K_2S_N2}$ in case of a bimolecular reaction and, therefore, the percentage content of the olefin formed drop sharply as the reagent is changed from $AlkO^-$ to $Br^-$ (in the latter case it is equal to 0) in agreement with theoretical suppositions.

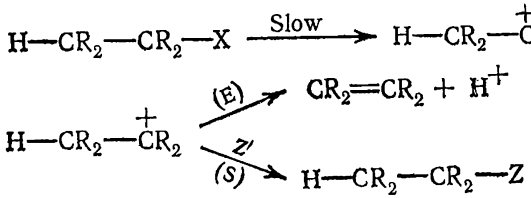
That is why the conversion of halides to alcohols is sometimes accomplished by first converting them to acetate esters and then hydrolyzing the latter to alcohols, rather than by treating the halides with caustic alkali (which would result predominantly

in olefins):

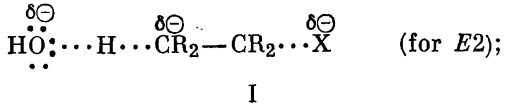



**Polarity of the Solvent.** As in the case of substitution reactions, the change of one solvent for another of higher ionizing power favours a change of the reaction mechanism from $E2$ to $E1$.

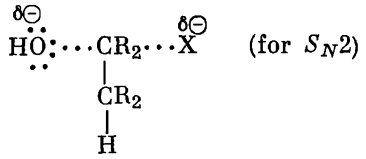
For monomolecular processes the ratio of elimination to substitution reactions $\frac{E}{S}$ does not depend on the nature of the solvent but is mainly determined by the basic structure of the cation formed during the first step of the reaction:




A much more complex picture is presented in bimolecular reactions where the $E/S$ ratio depends on the ratio of activation energies of the two corresponding active complexes, for instance,




I




II

Transition state II differs from transition state I in that the negative charge is less spread (over two atoms—O and X).

Although an increase in the ionizing power of the solvent will slow down both the $E2$ and $S_N2$ reactions, the latter ($S_N2$) will be slowed down less, because polar solvents in general promote processes of separation and formation of localized charges.

Conversely, in the case of solvents of lower ionizing power the conditions are more favourable for the formation of transition state I, and consequently, for the formation of olefins.

The above discussion explains why alcoholic and not aqueous caustic should be used in preparing olefins from alkyl halides (alcohol is less polar than water).

The second reason for the higher olefin content in the reaction products is that the $C_2H_5O^-$ ion is more nucleophilic as compared with $OH^-$.

Thus, in the general case the ratio $\frac{E}{S}$ depends on the complex interdependence of four different mechanisms ($S_N1$, $E1$, $S_N2$, $E2$), and prediction of results is thus very difficult. But in some cases this situation may be simplified. Thus, when carrying out reactions in acid solution favouring monomolecular reactions it is sometimes possible to deal with only two variables—the $S_N1$ and $E1$ rate constants. For example, in acidified aqueous-alcoholic solutions of 2-bromooctane, bimolecular reactions proceed to an insignificant extent, $S_N1$ takes place to 90.3% and $E1$ to 9.7%.

It can also be foreseen that the simplifying action of strongly alkaline solutions will favour bimolecular reactions.

Naturally, the structure of the compounds under consideration is of prime importance. By varying the structure a monomolecular or a bimolecular mechanism can be made to predominate.

It should be noted that in many textbooks and guides on organic chemistry statements are sometimes made regarding the ease of hydrolysis of alkyl halides and the ease of dehydrohalogenation; these statements are generally erroneous.

By way of example we may cite the following two statements:

1. *Elimination of hydrogen halides through the action of an alkali is easier from secondary alkyl halides than from primary, and from tertiary than from secondary alkyl halides.*

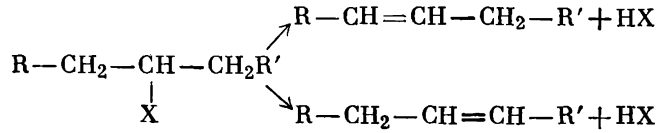
This statement is true only for certain concentrations of alkalies. If 0.05 $N$ caustic is used, hydrogen bromide is eliminated more easily from $(CH_3)_2CH$—Br than from $(CH_3)_3$ C—Br (see page 186).

2. *Tertiary alkyl halides are hydrolyzed more readily than secondary ones and secondary alkyl halides, more readily than primary ones; hydrolysis of alkyl halides is accelerated by the addition of an alkali.*

This statement is true only under definite conditions of hydrolysis and for halides of certain structure. But the general laws of hydrolysis (or more broadly, solvolysis) of alkyl halides are much more complex, as is evident from the above discussion.

## 3-5 DIRECTION OF ELIMINATION REACTIONS

A very important question is that of the factors influencing the direction of elimination when olefins of different structures may result, for instance:



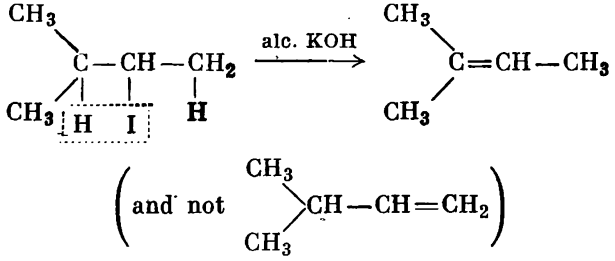
There are two empirical rules determining the predominant direction of elimination reactions—Zaitsev's rule and Hofmann's rule.

**Zaitsev's Rule.** *When hydrogen halides are eliminated from alkyl halides, hydrogen leaves the least hydrogenated carbon atom.*

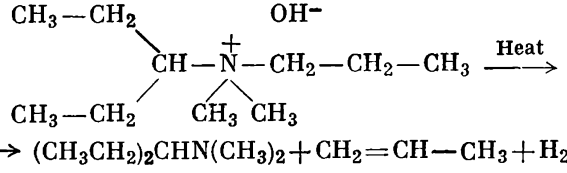
The same rule may be formulated differently:

*When an alkyl halide is converted to an olefin, the most alkylated of the two possible ethylenes is formed.*

The following reaction will illustrate this rule:



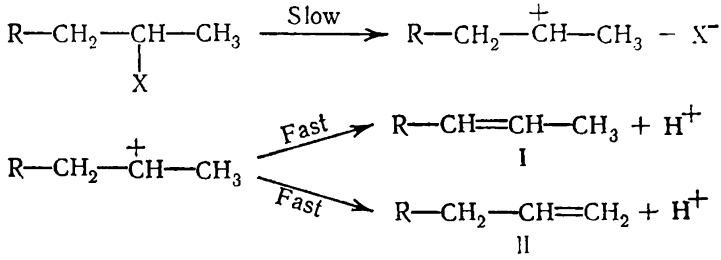
**Hofmann's Rule.** *When quaternary ammonium bases are decomposed, that olefin forms whose unsaturated carbon atoms are linked to the least number of alkyl groups (the least alkylated ethylene):*



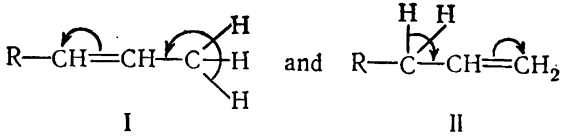
Experimental verification of the two rules showed that Zaitsev's rule holds for reactions following both $E1$ and $E2$ mechanisms, while Hofmann's rule applies only to reactions following an $E2$ mechanism. Decomposition of quaternary ammonium hydroxides according to an $E1$ mechanism follows Zaitsev's rule.

Hence, Zaitsev's rule is more general in nature. Theoretically, both rules may be interpreted as follows.

In the case of elimination reactions of hydrogen halides which follow an *E*1 mechanism, for example, from the compound R—$CH_2$—CH(X)—$CH_3$ two olefins may form:

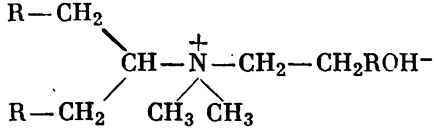



Inasmuch as olefin I is more stabilized by the conjugation of H — C and C = C bonds than olefin II (a minimum of three bonds being conjugated with the double bond in olefin. while in olefin II only two C — H bonds are so conjugated), it possesses less energy:

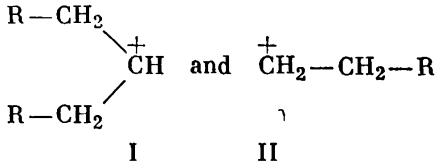



It follows from the above that the predominant reaction will be the formation of olefin I which is thermodynamically more feasible.

When quaternary ammonium hydroxides of the general type:



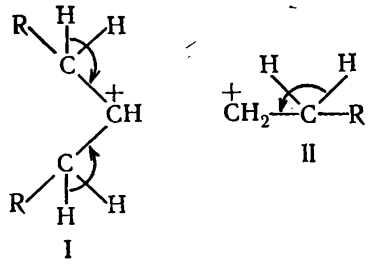

are decomposed according to an *E*1 mechanism the reaction formally may proceed in two directions to form the cations




respectively.

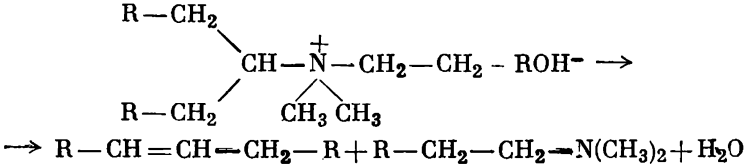
Cation I will possess less energy because its positive charge is more spread out, owing to the interaction of this charge with the

σ electrons of the α-C — H bonds:



I II

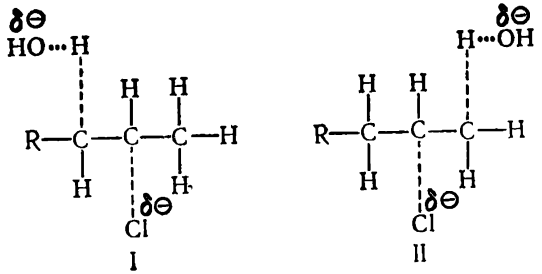
For this reason cation I will form more easily than cation II and, therefore, the reaction will proceed predominantly according to Zaitsev's rule:



Theoretical interpretation of these rules becomes more complicated when the elimination reactions follow an *E*2 mechanism, because in this case different olefins are formed depending on the kind of starting materials (halogen derivatives or onium compounds).

Theoretical interpretation of Zaitzev's rule is simpler.

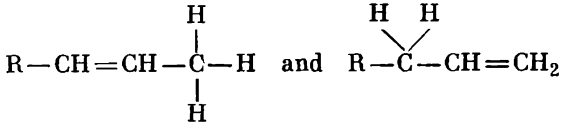
For the elimination of hydrogen halide from a general type of halogen derivative, $R - CH_2 - \underset{\displaystyle X}{\underset{|}{CH}} - CH_3$, two transition states are possible according to the *E*2 mechanism:



I II

Since there are no grounds to consider the energy states I and II to differ essentially from each other, it is natural to assume that the direction of the elimination reaction should depend mainly

on the thermodynamic factor—on the energy of the olefins formed:

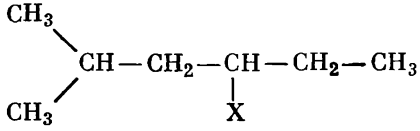


I II

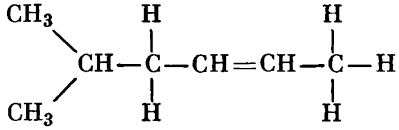
It is not difficult to arrive at the conclusion that olefin I possesses less energy, and will therefore be the main one to form from R — $CH_2$ — CHX — $CH_3$.

Thus, on the basis of the data discussed above a general rule may be formulated, according to which *elimination of hydrogen halides from alkyl halides results in the olefins which contain the greatest number of α-hydrogen atoms relative to the double bond.*

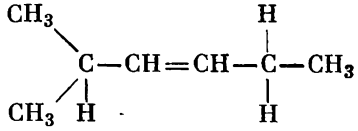
Therefore, when HX is eliminated from the alkyl halide



it is to be expected that the olefin



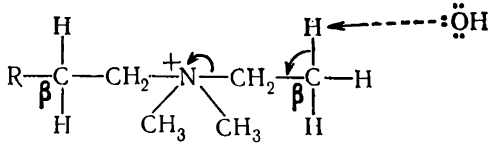
will form more readily than the olefin



because the first has 5 α-hydrogen atoms and the second only 3.

In the case of reactions of decomposition of onium compounds taking place according to *E*2 mechanisms the nature of the electronic factors determining the direction of the reactions has been studied insufficiently.

An important part in this case is probably played by steric factors. In the general case the attack is at the β-location which is less hindered sterically, e.g.:



As a result, the less alkylated ethylene forms in agreement with Hofmann's rule.

It is clear that thermodynamic stability of the reaction products is a factor of secondary importance in reactions proceeding according to Hofmann's rule, because the olefin that forms predominantly in this case is the less stable one, e. g. [5]:

$$C_2H_5-\underset{\displaystyle CH_3}{\underset{|}{CH}}-\overset{+}{S}(CH_3)_2 \xrightarrow{C_2H_5O^-} C_2H_5-CH=CH_2 + CH_3-CH=CH-CH_3$$

74% 26%

What factors may be decisive in this case?

First of all, it must be stated that if the reaction proceeds according to Hofmann's rule, the more acid hydrogen atom is eliminated as proton.

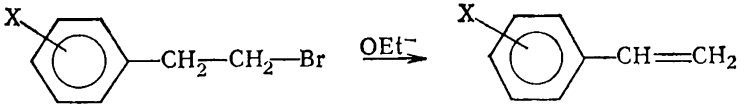
For example, of the five β-hydrogen atoms of compound III, the two hydrogens of the methylene group are markedly less acidic owing to the positive induction effect of the alkyl group

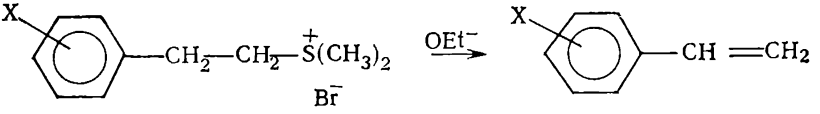
$$Alk \longrightarrow \underset{\beta}{\underset{|}{\overset{H}{\overset{|}{C}}}}-\underset{\alpha}{CHX}-\underset{\beta}{\underset{|}{\overset{H}{\overset{|}{C}}}}-H \quad [X=\overset{+}{N}(CH_3)_3,\ \overset{+}{S}(CH_3)_2]$$

*less acid* *more acid*

For this reason it seems that proton would preferably split away from the methyl group.

To get an insight into the mechanism of *E*2 reactions, the individual effect of the substituents must generally be taken into account, as they are of definite importance for this mechanism. For example, the rate constants of reactions (a) and (b)

(a) 

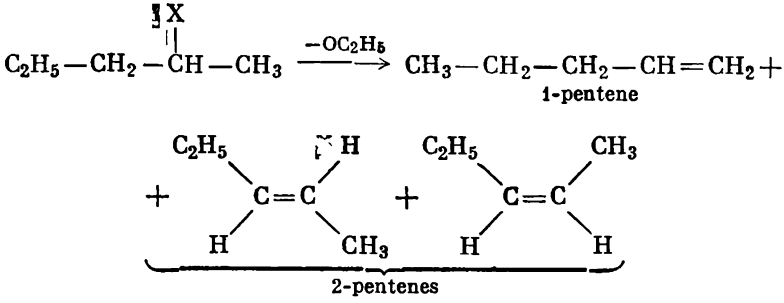
(b) 

were found [6] to be correlated with the values of the Hammett constants σ for their substituents X (these values being a measure of the electron-donating capability of the substituents). Reaction (b) turned out to be more sensitive ($\rho = 2.7$) to polar effects than

reaction (a), for which ρ was found to equal 2.1 [4b]. However, the difference between the ρ values is very small, and gives no grounds at all to conclude that among the totality of factors (conjugation and steric) the role of the induction effect should be determining for reactions of sulphonium compounds (b) and not so for those of alkyl bromides (a).

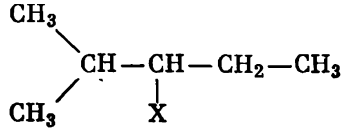
Steric factors are more pronounced in *E*2 reactions according to Hofmann because in these elimination reactions the leaving groups [$-\overset{+}{S}(CH_3)_2$, $-\overset{O^-}{\underset{O^-}{\overset{|}{\underset{|}{S^{++}}}}}-CH_3$, $N(CH_3)_3$] are undoubtedly more voluminous than the halide ions split off in Zaitsev reactions.

The importance of this factor is confirmed, for instance, by the fact that in *E*2 reactions of pentanes substituted in the 2-position the "Hofmann product" fraction in the olefin mixture increases as the leaving group X grows larger [7]:

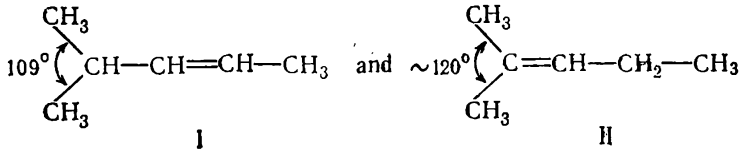



| X = | $Br$ | $\overset{+}{S}(CH_3)_2$ | $SO_2CH_3$ | $\overset{+}{N}(CH_3)_3$ |
|---|---|---|---|---|
| $\frac{\text{1-pentene}}{\text{2-pentene}}$ = | 0.45 | 6.7 | 7.7 | ~ 50 |

Steric hindrance apparently often plays an important part in alkyl halide elimination reactions. Thus, when hydrogen halide is eliminated from the compound



of the two olefins formed:

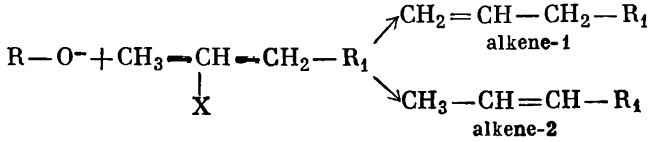


I II

olefin I will be more strained because the methyl groups, which have a definite volume, are closer to each other. Therefore, olefin II must form more readily due to both electronic and steric factors.

On the other hand, the direction of bimolecular eliminations is influenced by steric hindrances caused by the structure of the attacking nucleophilic reagent [8].

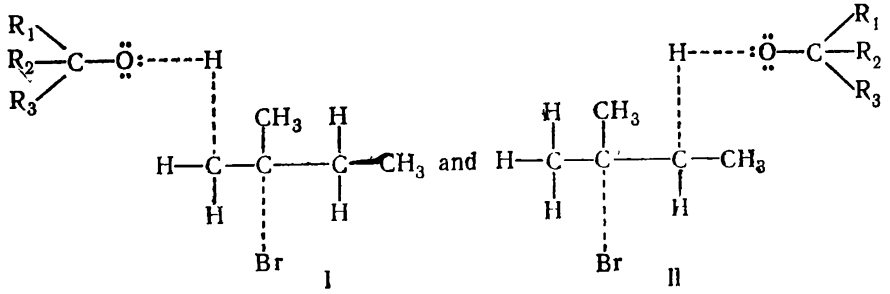
For instance, in the reaction of potassium alcoholate with alkyl halides:



alkene-1 alkene-2

the alkene mixture formed contains the more alkene-1, the more highly branched is R. Thus, 29% alkene-1 is formed in the reaction of *tert*-amyl bromide with potassium ethylate, 72% in that with potassium *tert*-butylate and 89% alkene-1 in that with potassium *tert*-amylate.

These results can be readily understood, since of the two transition states I and II:

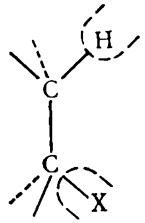


I II

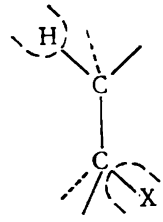
transition state II will become more difficult to achieve as the volume of the alcoholate ion increases, and the percentage of alkene-2 will become lower. Thus, owing to steric hindrance the bimolecular elimination of hydrogen halides from alkyl halides will take place, contrary to Zaitsev's rule, in the case of nucleophilic reagents with highly branched carbon skeletons.

## 3-6 STEREOCHEMISTRY OF ELIMINATION REACTIONS

Theoretically, in saturated compounds elimination reactions may take place from *cis*- or from *trans*-positions:




Cis elimination



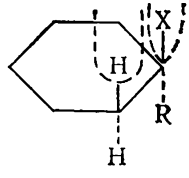

Trans elimination

Owing to the free rotation around the C — C bond in acyclic compounds it is impossible to determine the actual stereochemistry of the elimination reaction by direct experiment.

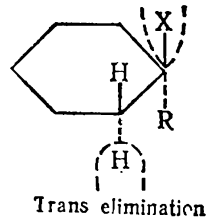
However, this can be accomplished with alicyclic compounds in which free rotation is restricted.

Besides elimination reactions of saturated alicyclic compounds, we shall consider below elimination reactions of olefinic compounds, which are similar in results, but probably very different in mechanism.

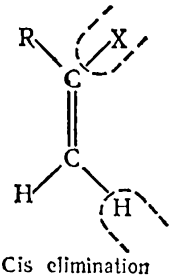
If alicyclic or ethylenic compounds in which the free rotation around the C — C bond is impeded undergo elimination reactions, two possibilities of the steric course of these reactions appear



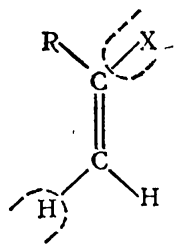

Cis elimination




Trans elimination



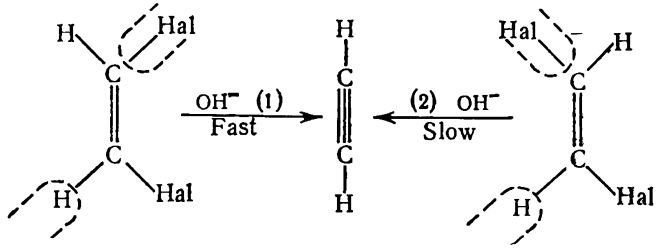

Cis elimination



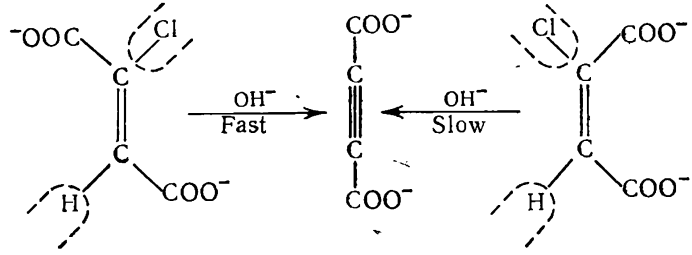

Trans elimination

Available experimental evidence shows that *trans*-elimination occurs more readily than *cis*-elimination.

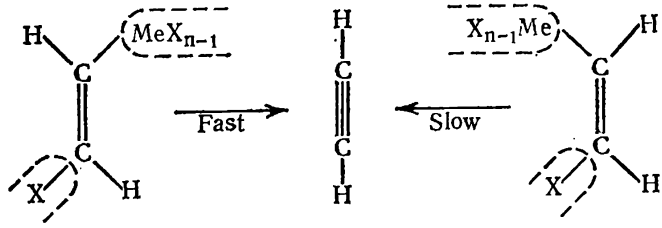
Thus, in the simplest case of isomeric dihaloethylenes, the *cis*-form will split out a hydrogen halide when treated with an alcoholic alkali, much faster than the *trans*-form:




The rate of reaction (1) is 20 times higher than that of (2) for dichloroderivatives, 135 times for dibromides, and 200 times for diiodides [9]. Alkalies convert chlorofumaric acid to acetylenedicarboxylic acid 50 times faster than they do chloromaleic acid:



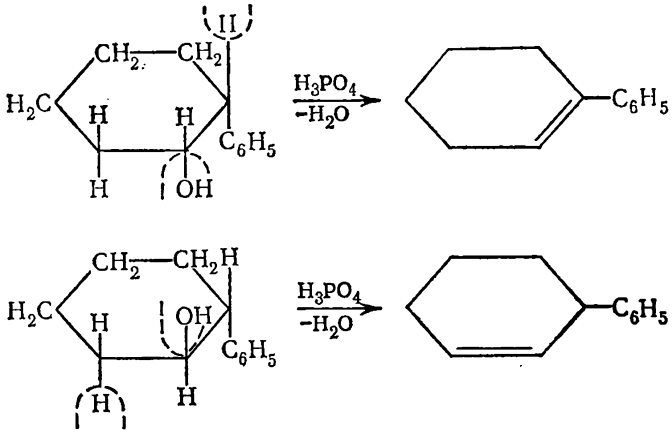

It is known [10] that the *cis*- and *trans*-isomers of chlorovinyl organometallic compounds differ considerably in ease of elimination of a metal halide (under the influence of such reagents as $Na_2S_2O_3$, NaI and other binders of metal halides):




*Trans*-isomers require less drastic conditions for this reaction.

Greater ease of *trans*-elimination reactions is characteristic of alicyclic compounds.

Thus, the tertiary hydrogen atom in 1-phenylcyclohexanol-2 can be split off by phosphoric acid only if it is *trans* to the hydroxyl group:

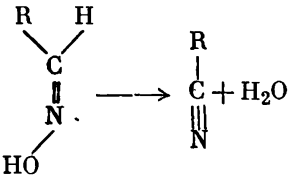


In the second case the tertiary hydrogen which is in *cis*-position to the hydroxyl is not split off despite the fact that this reaction would have resulted in the formation of a stable phenylcyclohexene with its double bond conjugated with the benzene ring.*

It is natural to suppose that the stereochemical peculiarities cited above must depend on the elimination reaction mechanism and that the rules determining the stereochemistry of substitution reactions at the saturated carbon atom (pages 121, 126), must have a close analogy in elimination reactions.

Interesting data were obtained in a study of the elimination of hydrogen chloride from isomeric hexachlorocyclohexanes by alkali in 80% aqueous alcohol. It was shown that the bimolecular elimination reaction proceeds readily for the isomers with their 1, 2 H and Cl atoms in *trans*-position. With the β-isomer, in which all the 1, 2 H and Cl atoms are in *cis*-positions, the elimination is much more difficult (7,000-24,000 times slower than with the other isomers); this

* *Trans*-elimination is easier only when the atoms or groups of atoms are eliminated from two neighbouring carbon atoms. An analogous condition is found in nitrogen compounds. Thus, water can be eliminated easily from aldoximes only if the H and OH are in a *trans*-arrangement:



fact indicates definitely that in the case of the β-isomer the stereochemical conditions for the elimination reaction are not fulfilled.

Kinetic investigations of five isomeric hexachlorocyclohexanes (α, β, γ, δ, ε), the formulas of which are given below, showed that in the case of the α-, β- and ε-isomers the rate-determining step of the reaction is the splitting off of the first molecule of hydrogen chloride, while for the γ- and δ-isomers the elimination of both the first and the second hydrogen chloride molecules takes place with measurable velocity making it possible to isolate the intermediate pentachlorocyclohexenes. All the reactions investigated, including the slow reaction of β-isomer, are second-order processes with activation energies of 19-21 kcal/mole, exclusive of the β-isomer, where it is 31-32 kcal/mole. The 11-12 kcal/mole higher energy of activation is evidently related to the fact that in this case the reaction starts with elimination of the proton and the formation of a kinetically independent carbanion of the type discussed on page 180.

This was proved by carrying out the reaction to 50% completeness in a deuterated solvent, whereupon the unreacted β-isomer was found to be partly deuterated [11, 12].

***Activation energy (in kcal/mole) of second-order reactions of hydrogen chloride elimination from hexachlorocyclohexanes with alkali in aqueous ethanol***

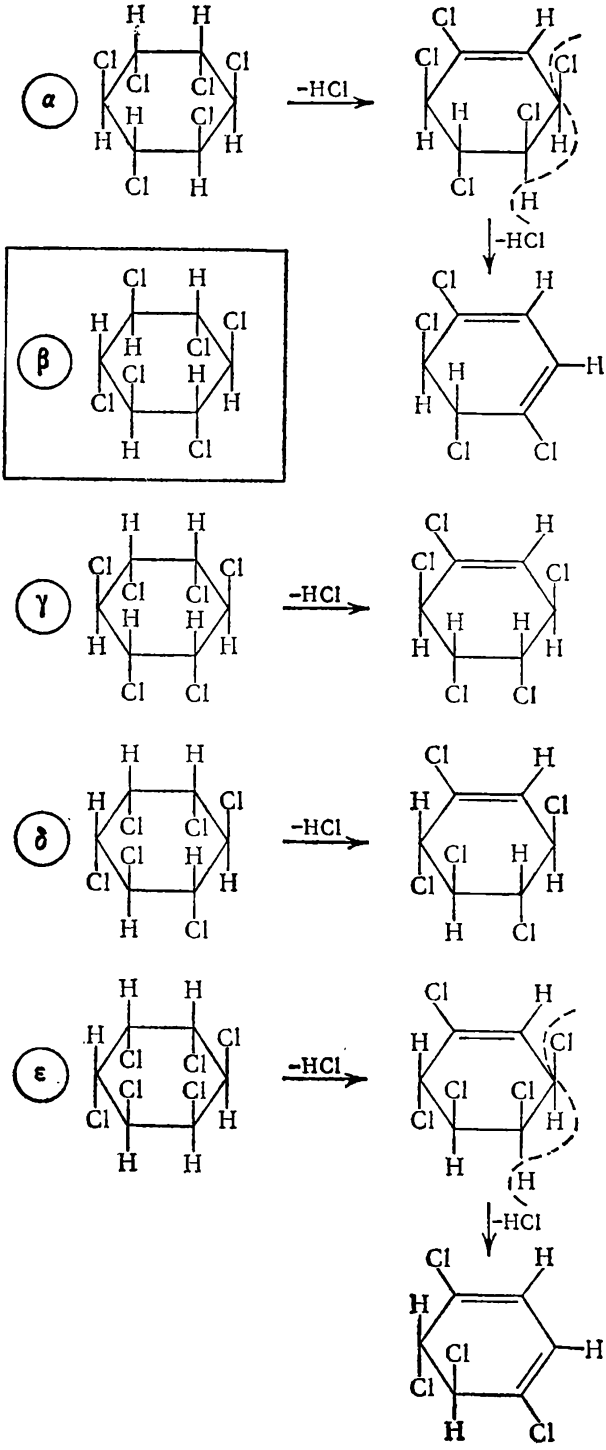
| Structure of isomer: position of *cis*-chlorine atoms | 1,2,4 | 1,3,5 | 1,4 | 1,3 | 1,2,3 |
|---|---|---|---|---|---|
| Step of reaction . . | 1st | 1st | 1st, 2nd | 1st, 2nd | 1st |
| In 90% ethanol . . . | 19.0 | 32.3 | 20.4; 20.1 | 21.6; 21.1 | — |
| In 80% ethanol . . . | 18.5 | 31 | (20.6) | — — | 21.4 |

That the rate of reaction is controlled by both steps in only two of the isomers may be understood by assuming that second-order *trans*-elimination with participation of an allylic chlorine atom takes place much faster than with the participation of an ordinary alkyl chlorine atom.

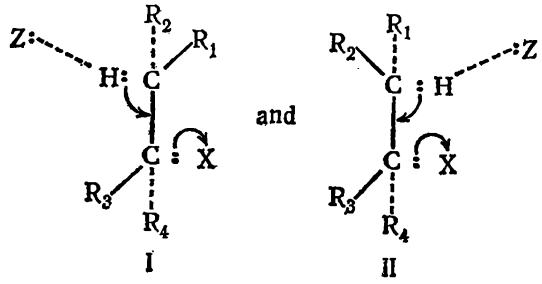
Leaving out of consideration the β-isomer, for which the mechanism of hydrogen chloride elimination is not yet clear, it can easily be seen that elimination of the second HCl molecule must involve an allyl chlorine atom (fast), in the case of the α- and ε-isomers, and an alkyl chlorine atom (slow) in the case of the γ- and δ-isomers. Hence the appearance in the latter case of the second stage determining its reaction rate.

From all the experimental data available on elimination reactions a rule evolves, according to which *if the reaction follows a bimolecular (E2) mechanism, trans-elimination takes place.*

A theoretical explanation of this rule may be given by considering the corresponding transition states. For systems with free rotation

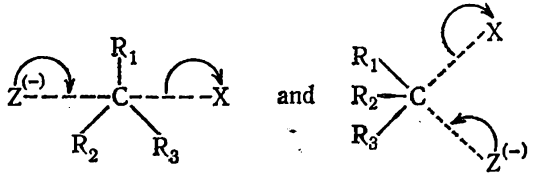

α
-HCl
-HCl
β
γ
-HCl
δ
-HCl
ε
-HCl
-HCl

around the C — C bond two transition states are possible:




I II

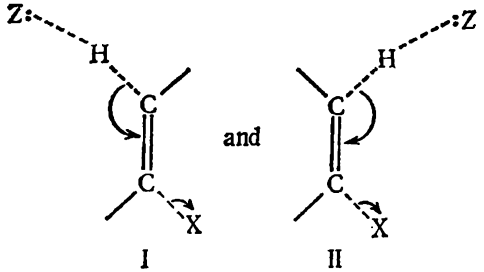
The activation energies necessary for the transition states I and II are not equal, being smaller for I because this state involves less energy of repulsion of the electronic pairs H — Z and C — X (which are situated farther away from each other than in transition state II). As a result of this, transition state I will be the predominant one, and the bimolecular elimination reaction will be one of *trans*-elimination. As was previously established (page 120) an analogous condition exists in the case of bimolecular nucleophilic substitution where of the two possible transition states:




I II

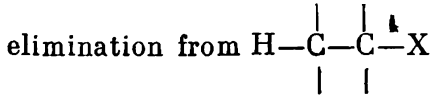
only transition state I is valid because the energy of repulsion of electronic pairs is smaller.

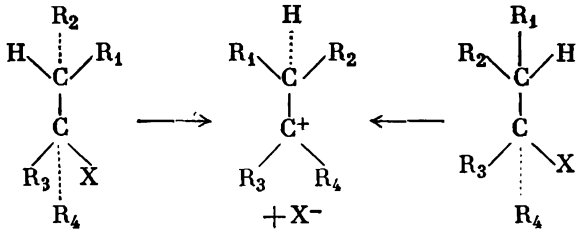
In the case of compounds lacking free rotation a similar conclusion can be reached apparently by considering the following two transition states:



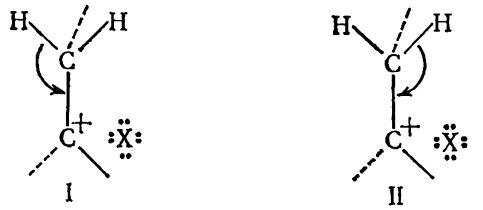

I II

Such an examination, however, cannot, strictly speaking, be considered substantiated, because the substitution and elimination mechanisms of unsaturated compounds differ from those of saturated compounds. Here too transition state I corresponding to *trans*-elimination must possess less energy (because of the smaller energy of repulsion of electronic pairs), and therefore the elements HX will be eliminated from *trans*-positions.

In *E*1 reactions of monomolecular elimination from  systems the carbonium ion must assume a flat configuration if it lasts long enough, owing to which the elimination will not depend on the initial (rotary) configuration:



However, if the elimination ends before the dissociated group X gets far enough away and the cation assumes a planar configuration, then *trans*-elimination will predominate for the same reason as in bimolecular elimination (less energy of repulsion of electronic pairs in the transition state):

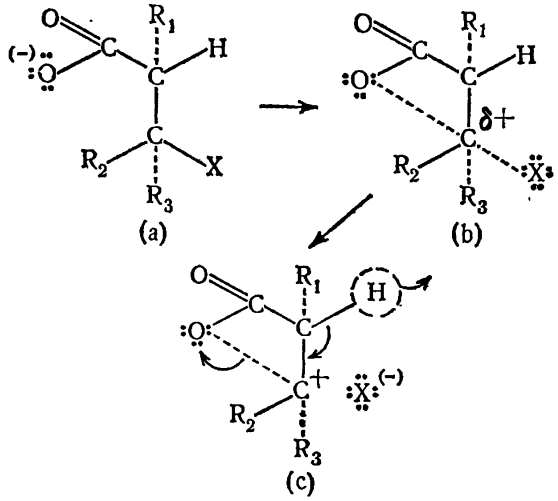


I — Less energy

II — More energy

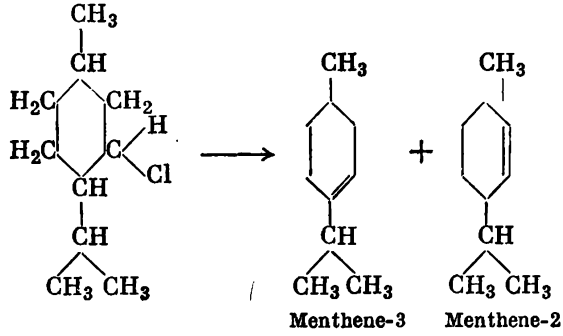
If, however, the nucleophilic group is so positioned that it can stabilize the configuration of the carbonium ion until the elimination is over, then *cis*-elimination will predominate, for

example:




In the process of ionization of X the negatively charged carboxyl ion interacts with the positively charged carbon atom and fixes the configuration of the carbonium ion, preventing free rotation along the C — C bond, so that only *cis*-elimination (*c*) is possible.

Data are given below on the influence of polar orientation and steric factors on the elimination reaction of hydrogen chloride by alcoholic alkali from menthyl chloride and neomenthyl chloride in alcoholic solution:




*Bimolecular elimination*

1. Neomenthyl chloride + $OC_2H_5^-$ $\xrightarrow{E2}$ Menthene-3 + Menthene-2
   [*trans*-(*tert*-H) (Cl)] ~ 75% ~ 25%
   In accordance with Zaitsev's rule

2. $\left\{\begin{array}{l}\text{Menthyl chloride} + OC_2H_5^- \\ \text{[}cis\text{-(}tert\text{-H)(Cl)]}\end{array}\right. \xrightarrow[E2]{} \begin{array}{ll}\text{Menthene-3} + \text{Menthene-2} \\ 0\% \qquad 100\%\end{array}$

**Contrary to Zaitsev's rule**

*Monomolecular elimination*

3. $\left\{\begin{array}{l}\text{Menthyl chloride} \\ \text{[}cis\text{-(}tert\text{-H)(Cl)]}\end{array}\right. \xrightarrow[E1]{} \begin{array}{ll}\text{Menthene-3} + \text{Menthene-2} \\ \sim 70\% \qquad \sim 30\%\end{array}$

In accordance with Zaitsev's rule

If the direction of a bimolecular elimination reaction is determined by polar effects, then it must correspond with Zaitsev's rule. Actually, in the case of neomenthyl chloride, where the hydrogen attached to the tertiary carbon atom and the secondary hydrogen atom are in a *trans*-position to the chlorine, the elimination proceeds according to Zaitsev's rule. However, in the case of menthyl chloride, where the chlorine atom and the tertiary hydrogen are in *cis*-position, the bimolecular elimination reaction goes entirely contrary to Zaitsev's rule (the chlorine atom takes the *trans*-H from the methylene group) and results in menthene-2. The rate of the second-order hydrogen chloride elimination reaction is in this case 200 times lower than for neomenthyl chloride, testifying to the unfavourable electrochemical direction of the reaction.

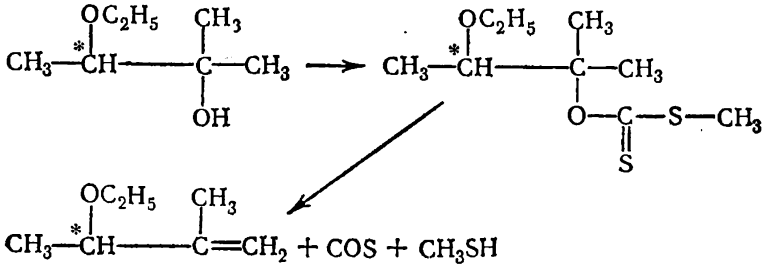
In the case of monomolecular elimination of hydrogen chloride from menthyl chloride, however, steric factors do not influence the direction of the reaction substantially; the latter is determined by polar orientation. As a result, monomolecular elimination of hydrogen chloride from menthyl chloride follows Zaitsev's rule. The cited examples illustrate the complex interrelationships of the polar and steric factors influencing the course of elimination reactions.

**Chugaev's Reaction.** L. A. Chugaev discovered a peculiar reaction of conversion of alcohols to olefins by thermal decomposition of xanthate esters derived from the alcohols [13]. The peculiarity of this reaction when compared with other methods of dehydration consists in that the alcohols dehydrate without any change in the carbon skeleton.

Thus, dehydration of pinacol yields 2,2-dimethylbutene-3:

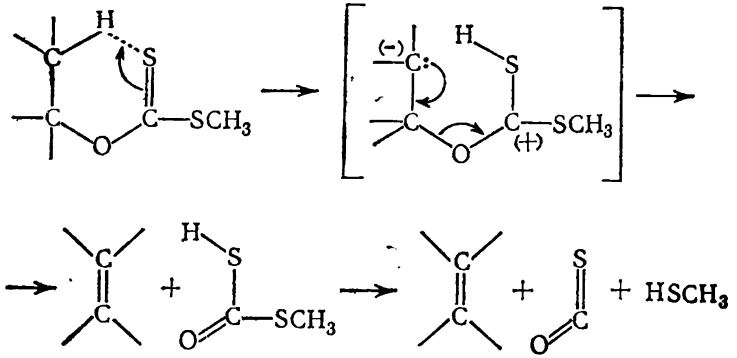
$$(CH_3)_3C-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_3 \longrightarrow (CH_3)_3C-\underset{\displaystyle O-C-S-CH_3}{\underset{|}{CH}}-CH_3 \longrightarrow$$
$$\qquad\qquad\qquad

and dehydration of optically active 2-methyl-3-ethoxybutanol-2 results in optically active 2-methyl-3-ethoxybutene-1:



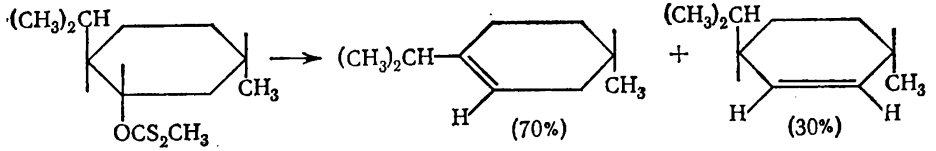
This reaction was of particular value in the investigation of terpenes.

The mechanism of Chugaev's reaction was studied but little [1]. A hypothesis was put forth according to which the decomposition of xanthate esters is initiated by the intramolecular hydrogen bond between the sulphur atom and the β-hydrogen atom:

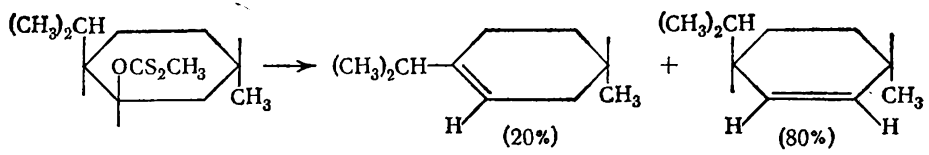


This hypothesis concerning the reaction mechanism is borne out by the fact that when xanthogenates decompose the *cis*-hydrogen atom is eliminated predominantly.

Thus, 1-menthylxanthogenate forms 70% of menthene-3 and 30% of menthene-2, while the decomposition of *d*-neomenthylxanthogenate yields 80% of menthene-2 and 20% of menthene-3:



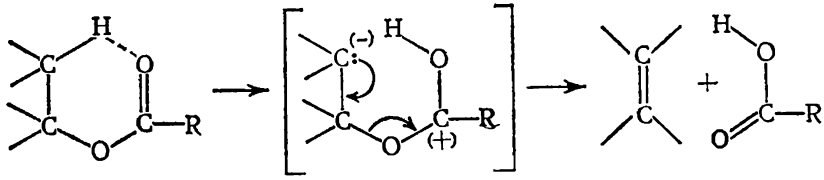
[1] The possibility of Chugaev's reaction following a radical mechanism cannot be excluded.




In other cases studied hydrogen was also eliminated predominantly from the *cis*-position.

It is obvious that the Chugaev reaction produces results opposite to those obtained in dehydrations effected through the action of sulphuric or phosphoric acids (page 198).

A similar mechanism has been suggested for the pyrolysis of carboxylic acid esters:




The reason why *cis*-elimination occurs in the Chugaev reaction and in the pyrolysis of carboxylic acid esters is not clear. A possible explanation is that in these cases the energy evolved during the formation of weak hydrogen bonds by *cis*-hydrogen atoms exceeds the difference of the energies of repulsion of electronic pairs in *cis*- and in *trans*-elimination, respectively.

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# 4

# ADDITION TO UNSATURATED COMPOUNDS

## 4-1 ADDITION TO MULTIPLE CARBON-CARBON BONDS (C=C AND C≡C)

Addition of halogens, hydrogen halides, sulphuric acid, salts of heavy metals and other reagents, oxidation and polymerization are characteristic reactions of the alkene series.

There is experimental evidence to the effect that activating factors are necessary for the materialization of reactions of addition to ethylene compounds.

Thus, the addition of bromine vapours to ethylene takes place at the walls of the vessel exclusively and the rate of this process depends on the nature of the wall surface [1]. If the reaction is carried out in a vessel with coatings of various substances on its walls, the rate of the addition reaction diminishes in the following sequence: stearic acid > glass > cetyl alcohol > wax, that is, it decreases as the surface becomes less polar. The rate of addition in a vessel with wax-coated walls is 1/17 of its value in a regular glass vessel.

The reaction between bromine and ethylene proceeds very slowly in the dark in clean dry carbon tetrachloride (taking hours, even days, to go to completion); however, small quantities of moisture or illumination accelerate it considerably [2]. Thus, addition reactions in the liquid phase also require a definite activation of the alkene.

These facts suggest that addition to the double bond is preceded by activation of the latter—shifting of the π-electron pair toward one of the carbon atoms:

It is not impossible that polarization of the halogen

$$X{:}\,X \rightarrow \overset{\delta\oplus}{X} \ldots \ldots \overset{\delta\ominus}{:X}$$

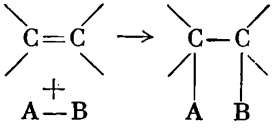
also plays an important (perhaps cardinal) part.

When studying the mechanism of addition reactions to the carbon-carbon double bond, it should be taken into consideration that the great variety of known reactions of this type makes it highly improbable that all these processes follow a single mechanism. Therefore, we should confine ourselves to establishing rules which are generai for definite types of addition reactions, without expecting these rules to be valid for all the addition reactions.

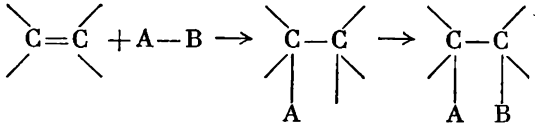
## 4-1.1 Electrophilic Addition to Unsaturated Compounds

### Electrophilic Addition of Halogens

When any molecule A — B adds to a double bond, two cases are possible. The parts of the molecule A and B may add either simultaneously

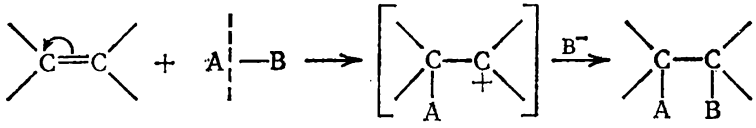


or stepwise



### Stepwise Reaction Mechanism of Electrophilic Addition

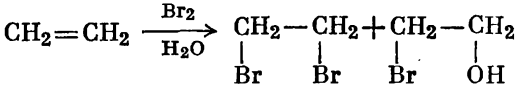
At present the stepwies mechanism of addition to double bonds may be considered proved:



Experimental data supporting this mechanism fall into two groups: data obtained as a result of the study of "mixed addition", and data obtained when studying the stereochemistry of addition reactions.

The following are the most important experimental facts obtained in the study of "mixed addition" [3]:

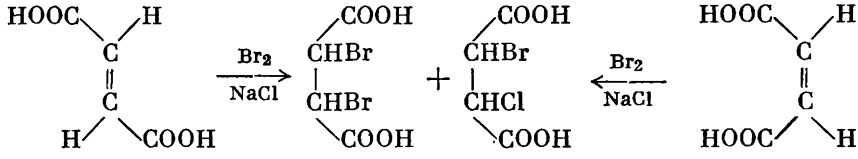
(1) the addition of bromine to ethylene in aqueous solution results in ethylene bromohydrin besides ethylene bromide



(2) if the reaction of ethylene with bromine is carried out in a concentrated aqueous solution of sodium chloride, chlorobromoethane is formed together with ethylene dibromide

$$CH_2=CH_2 \xrightarrow[NaCl]{Br_2} \underset{Br}{\overset{|}{CH_2}}-\underset{Br}{\overset{|}{CH_2}}+\underset{Br}{\overset{|}{CH_2}}-\underset{Cl}{\overset{|}{CH_2}}$$

(3) when bromine is added to fumaric and maleic acids in a concentrated aqueous solution of sodium chloride, chlorobromosuccinic acid results together with dibromosuccinic acid



(4) the addition of bromine to ethylene in a concentrated aqueous solution of sodium nitrate yields dibromoethane and bromoethyl nitrate

$$CH_2=CH_2 \xrightarrow[NaNO_3]{Br_2} \underset{Br}{\overset{|}{CH_2}}-\underset{Br}{\overset{|}{CH_2}}+\underset{Br}{\overset{|}{CH_2}}-\underset{ONO_2}{\overset{|}{CH_2}}$$

(5) in the reaction of stilbene with bromine in methanol, dibromostilbene and bromomethoxystilbene result

$$C_6H_5-CH=CH-C_6H_5 \xrightarrow[CH_3OH]{Br_2}$$
$$\rightarrow C_6H_5-\underset{Br}{\overset{|}{CH}}-\underset{Br}{\overset{|}{CH}}-C_6H_5+C_6H_5-\underset{Br}{\overset{|}{CH}}-\underset{OCH_3}{\overset{|}{CH}}-C_6H_5$$

(6) a similar reaction takes place when chlorine is added to acetylenic compounds in methanol

$$R-C\equiv CH \xrightarrow[CH_3OH]{Cl_2} R-CCl=CHCl+R-\underset{CH_3O}{\overset{|}{C}}=\underset{Cl}{\overset{|}{CH}}$$

(7) when chlorine is added to ethylene in acetic acid, β-chloroethyl acetate and ethylene chloride are formed

$$CH_2=CH_2 \xrightarrow[CH_3COOH]{Cl_2} \underset{Cl}{\overset{|}{CH_2}}-\underset{Cl}{\overset{|}{CH_2}}+\underset{Cl}{\overset{|}{CH_2}}-\underset{OCOCH_3}{\overset{|}{CH_2}}$$

The possibility of obtaining "mixed" reaction products in the first, fifth and sixth cases by the addition of hypobromous acid, methyl hypobromite and methyl hypochlorite, respectively, to the

unsaturated substance is out of the question because of kinetic considerations.

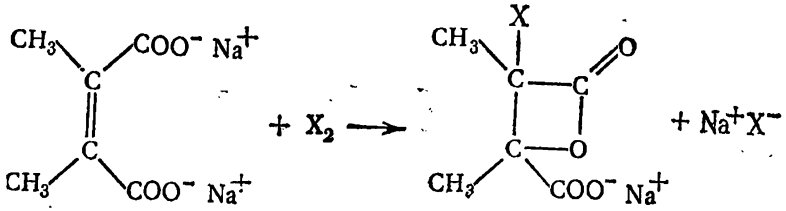
If the "mixed" reaction products formed as a result of the addition of HOX or its ethers to the olefin

$$Br_2 + H_2O \rightleftarrows HOBr + H^+ + Br^-$$

$$X_2 + CH_3OH \rightleftarrows CH_3OX + H^+ + X^-$$

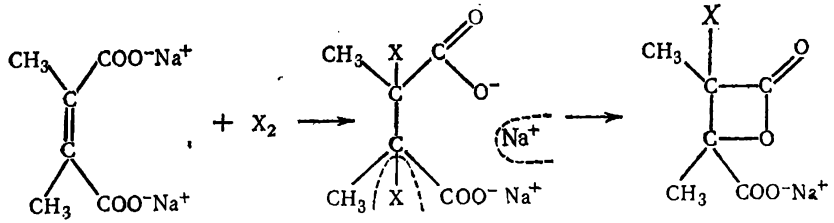
the percentage of the "mixed" products would decrease with growing hydrogen ion concentration. However, it has been established experimentally that the percentage of "mixed" reaction products is independent of the hydrogen ion concentration. At the same time it decreases when halogen ions are added, as was shown for the reaction of stilbene with bromine in methanol. This can be understood if $Br^-$ and $CH_3O^-$ additions are assumed to be competing processes.

In all the cases mentioned above the sources of anions competing with the halogen anions in the process of addition to the alkene were other substances added to the reaction mixture. However, cases are known where the nucleophilic group of the alkene itself served as the competing anion. For example, if bromine or chlorine is added to an aqueous solution of sodium dimethyl maleate, a β-lactone of dimethyl halomalic acid results



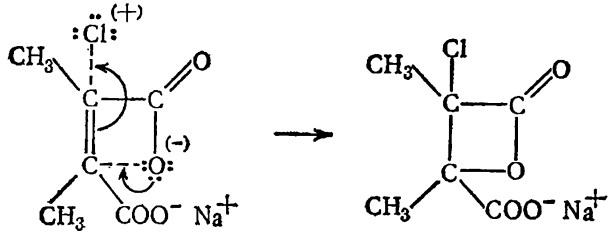
The reaction of sodium dimethyl fumarate proceeds analogously [4].

The assumption that the β-lactones were secondary products of conversion of the dihalide derivatives originally formed



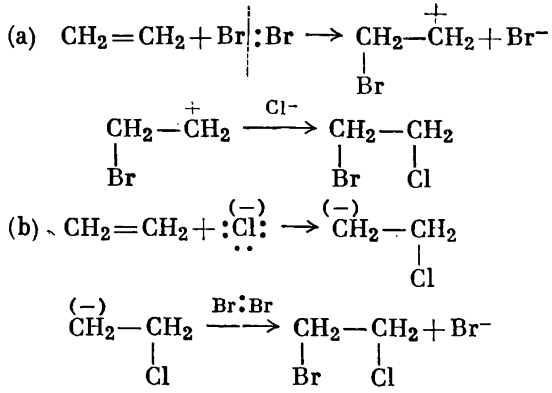
was erroneous because sodium dichloro (dibromo) dimethyl succinates do not yield lactones.

The only other assumption is that the formation of the lactone ring is caused by the carboxyl ion attacking the carbon atom

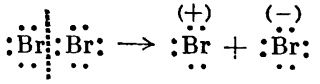


All the facts given above on "mixed" addition indicate convincingly that the two parts of the halogen molecule reacting with alkene do not add simultaneously because, if they did, no "mixed" products could have formed.

None the less, these facts are insufficient to decide which of the parts of the molecule adds first to the alkene: the cationoid (electrophilic) or the anionoid (nucleophilic) part. The formation, for example, of chlorobromoethane from ethylene and bromine in the presence of sodium chloride may be attributed to two equations:



Theoretical considerations show the first mechanism (a) to be the more likely one. According to it the first slow stage of the reaction consists of the addition of an electrophilic reagent ($Br^+$ in this case) to the double bond. This conclusion follows from the fact that heterolytic cleavage of the bromine molecule, which occurs either under the action of a catalyst or upon collision with an alkene molecule,



results in an electrophilic $Br^+$ and a nucleophilic $Br^-$ reagents, possessing different energies and, therefore, differing in reactivity.

The less stable and more reactive $Br^+$ may attack a neutral alkene molecule and add to its π-electron pair. The less reactive $Br^-$ is unable to join the neutral alkene molecule through its electron pair. But in the second ionic stage of reaction it adds readily to the cation formed after the addition of $Br^+$ to the alkene.

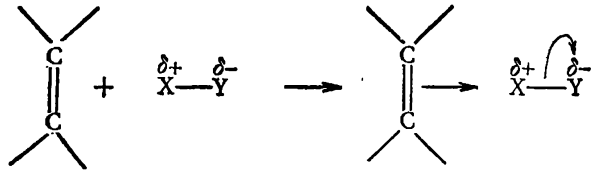
Results of kinetic investigations confirm that the electrophilic reagent adds first to the alkene in reactions of alkenes with halogens. In reactions of alkenes with hydrogen halides it has also been proved that proton is the first to add to the alkene.

This is confirmed by the fact that acids take part in such reactions while substances which give rise to halogen ions, are generally (except for hydrogen halides) not capable of addition to alkenes. Therefore, proton apparently participates in this important step of the reaction. The proton is not free, of course, but is bound somehow: in an ionizing solvent, it is solvated; in a nonpolar solvent, such as benzene, or in the absence of a solvent, it is probably linked with the halogen in the unionized molecule HX, or in the presence of a catalyst (say, $FeCl_3$) it may be a part of some complex.

The most convincing proofs that the proton adds first to alkenes were obtained in a kinetic study of the addition of HCl and HBr to cyclohexene and hexene-3 [5]. It was shown that in solvents capable of oxonium salt formation (ether, dioxane) the rate of addition was lower than in solvents incapable of proton binding (heptane, benzene). As only the first of the two reaction steps of the addition of HX to alkenes is a slow process (reaction of an ion with an alkene molecule), and the second step proceeds at the rate of ionic processes, it is obvious that retardation or acceleration of the addition reaction depends wholly on retardation or acceleration of the first stage of the reaction. Since the use of electrophilic solvents (ether, dioxane), which bind protons, retards the reaction, it is clear that proton adds in the first stage of the reaction.

### π-Complexes

In discussing reaction mechanisms of additions to the ethylene bond, Dewar developed concepts [6], according to which the first stage of the reaction consists in the formation of a complex between one molecule of the alkene and one molecule of reagent, these complexes being called π-complexes.




π-complex

A π-complex contains a coordination-type bond between the alkene molecule and the positively charged atom X of the X — Y molecule. The π-complex differs from the Roberts and Kimball cation [7] (see page 218), but in the course of the reaction it may be transformed into it.

If the alkene molecule is asymmetrical, the electron density of the coordination bond in the π-complex does not have a plane of symmetry perpendicular to the C — C bond. The positively charged atom X in such a π-complex is located closer to the carbon atom with the higher electron density (an important factor for the orientation of addition reactions).

Application of the method of molecular orbitals yields valuable information for an understanding of the nature of π-complexes [8].

π-Complexes play an important part as intermediates in many chemical reactions. In reactions of addition to the carbon-carbon double bond they play the following part: in the course of the reaction of addition to the double bond the carbon-carbon distance should increase from 1.33 Å to 1.54 Å (in the activated complex this distance should be intermediate between 1.33 and 1.54 Å). Increasing the interatomic distance requires the expenditure of a large amount of energy, which accounts for a large part of the activation energy. However, in the formation of a π-complex an increase of the interatomic carbon-carbon distance has already been effected due to the reaction with the positively charged X atom. This is responsible for the increased reactivity of the alkene.

### . Kinetics of Electrophilic Addition Reactions

The addition of halogens to alkenes in water, alcohol, aqueous acetic acid (and in glacial acetic acid, if the concentration of the halogen does not exceed ~0.001 *M*) is a second-order reaction. Admixtures of water and ionizing salts accelerate the reaction; this is understandable, because the reaction is heterolytic in nature. In acetic acid (but not in more polar solvents) the addition of bromine (in the concentration range around 1/40 *M*) takes place as a third-order reaction. Lowering the bromine concentration, increasing the temperature or adding water to the solvent change the kinetic order of the reaction to second order. The effect of the alkene structure (page 223) on the rate of this third-order reaction is the same as for a second-order reaction. These data indicate that in this case the third-order reaction differs insignificantly in mechanism from the second-order reaction, though a second halogen molecule participates in the transition state.

In acetic acid solution the addition of iodine, iodine bromide or chloride, and bromine chloride to alkenes are also third-order

reactions. The relative rates of addition of these reagents are as follows [12]:

| Halogen | $I_2$ | IBr | $Br_2$ | ICl | BrCl |
|---|---|---|---|---|---|
| Rate | 1 | 3,000 | 10,000 | 100,000 | 4,000,000 |

This sequence of addition rate values confirms that the first stage of the reaction of halogens with alkenes is addition of the cation. This follows from an examination of the electrophilic activity of the halogen molecules.

If the first stage of the reaction consists in the cation attacking the alkene, one would expect the rate of addition to increase in the following sequence:

$$I:I < \overset{\delta\oplus\ \delta\ominus}{I:Br} < \overset{\delta\oplus\ \delta\ominus}{I:Cl}$$

because bromine pulls electrons away from the iodine atom more vigorously than iodine in the first case, and chlorine pulls them away still more vigorously. This actually takes place.

That the rate of addition of ICl is lower than that of Br — Cl, though electrons are pulled away from the iodine atom (to form a cation) more easily than from the bromine, can be accounted for as follows: the first stage of the reaction—addition of the halogen cation to the alkene molecule—is a slow process, because the cation is reacting with a neutral molecule. Only a few of the collisions between the cations and the neutral molecules result in formation of a halogen-carbon bond. Therefore, the rate of the first and slowest reaction stage depends on the chemical activity of the halogen cation. The cation $Br^+$ is much more active than $I^+$. This is the decisive factor determining the higher rate of Br — Cl addition, in spite of the fact that the cation $I^+$ forms easier (from I — Cl) than $Br^+$ (from Br — Cl).

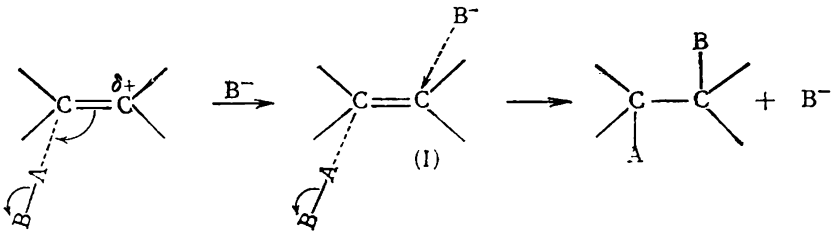
The addition of chlorine to alkenes is also a trimolecular reaction, the kinetics of which is expressed by the equation:

$$-\frac{d[Cl_2]}{dt} = K\left[\diagup\!\!\diagdown C{=}C\diagup\!\!\diagdown\right][Cl_2][Cl^-]$$

Probably, in the majority of cases addition reactions do not proceed as far as the formation of an intermediate carbonium ion with a whole positive charge $\left(\diagup\!\!\diagdown CA - \underset{+}{C}\diagup\!\!\diagdown\right)$, as shown on page 209.

Evidently, as soon as the cationoid end of the halogen molecule attacks the unsaturated carbon atom and a partial positive charge appears on the neighbouring carbon atom, the third component

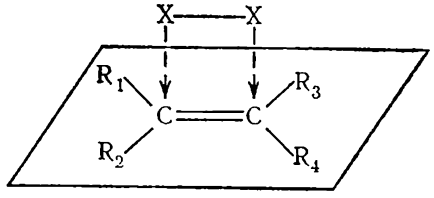
attacks instantaneously [13], resulting in the formation of a trimolecular transition complex (I):




**Stereochemistry of Electrophilic Addition Reactions**

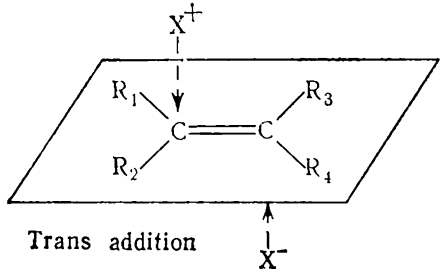
Investigation of the stereochemistry of addition reactions of alkenes also confirms the hypothesis of stepwise addition.

If both atoms of the halogen molecule add simultaneously to two carbon atoms of the alkene molecule, *cis*-addition should be expected:




Cis addition

If, on the other hand, it is assumed that the two halogen atoms do not add simultaneously, such a two-step addition may result in either *cis*- or *trans*-addition:

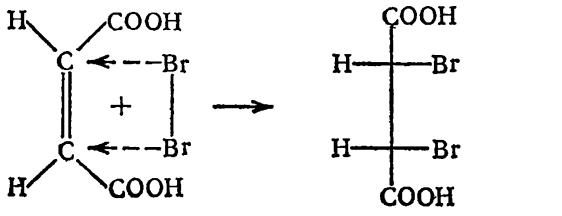


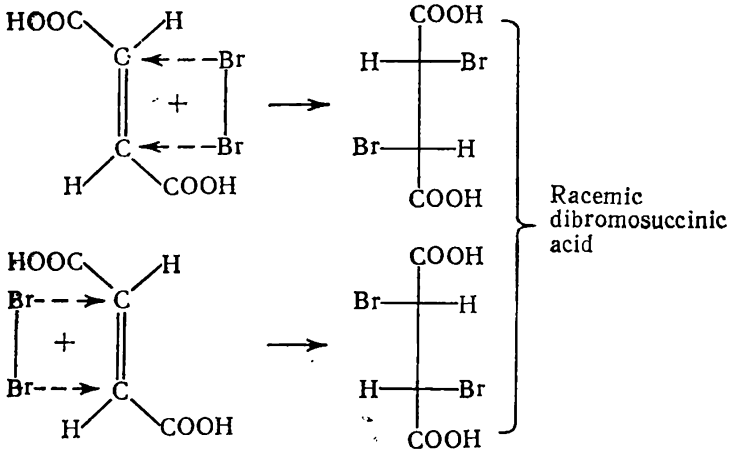

Trans addition

Experimental evidence shows that the addition of halogens to the double bond of alkenes is almost always *trans*-addition [14].

If this reaction were one of *cis*-addition, the addition of bromine to maleic acid, for instance, would result in the formation of mesodibromosuccinic acid, and the addition of bromine to fumaric acid,

in racemic dibromosuccinic acid:

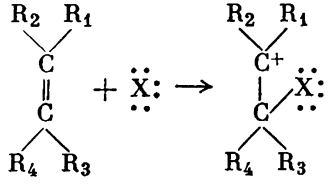



The facts are in contradiction with this assumption. In reality, the addition of bromine to maleic acid results in racemic dibromosuccinic acid and its addition to fumaric acid, in meso-dibromosuccinic acid, indicating *trans*-addition in both cases.

The most widely accepted explanation of this phenomenon is the following.

The reaction starts with addition of the halogen cation to the π-electron pair of the carbon-carbon double bond



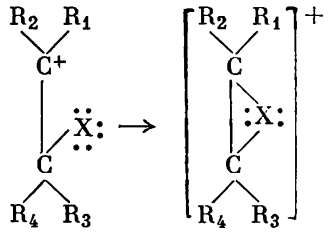

Since the trivalent positively charged carbon atom must assume a planar configuration and since rotation around an ordinary carbon-

carbon bond is generally easy, the *cis*- and *trans*-isomers of the unsaturated compound should give the same transition cation, and therefore the same final reaction products. However, as was shown above for maleic and fumaric acids, the reaction products are actually different.

To account for the absence of free rotation in this case a hypothesis was suggested at first, according to which the second reaction step—addition of the halogen anion—occurs so rapidly that free rotation cannot materially influence it.

Later, however, it was shown that this hypothesis is extraneous because no free rotation is to be expected at the transition cation.

As the cation contains a halogen atom with six valence electrons near the carbon atom carrying the positive charge, and as the ionization potentials of carbon and the halogens are close (C 11.24 eV, Cl 13.01 eV, Br 11.82 eV, I 10.43 eV), it is natural for bonds to form between the positively charged carbon and the halogen:




Cation I actually does not form as a kinetically independent particle; instead, cation II forms immediately: it contains a three-membered onium ring*, and is therefore incapable of free rotation.

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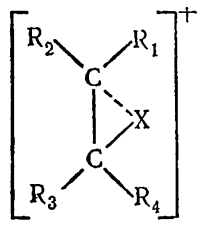
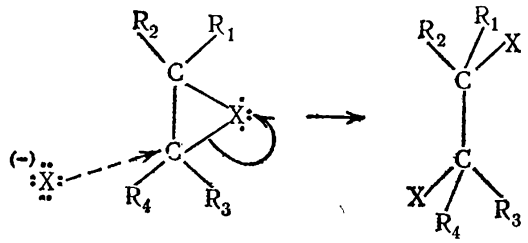
* The question of whether both the C—X bonds in cation II are equivalent is of no moment in this case. Even if the second bond is weaker than the first, its presence will still prevent free rotation:



The addition of the halogen anion $X^-$ to cation II with the formation of the end dihaloderivative proceeds like a bimolecular substitution reaction. The halogen anion attacks one of the carbon atoms of the three-membered ring, causing an inversion of configuration*:



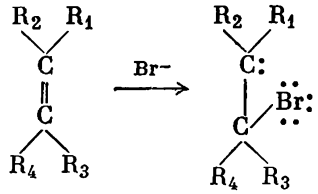
It is clear from the above discussion that reactions of halogens with alkenes, which follow such a two-stage mechanism are *trans*-additions**.

It is natural to expect that a three-membered onium ring formed with the participation of a halogen, would be unstable. It is possible to assume, for instance, that such a ring will break easily, or will not form at all if the substituents $R_1$ and $R_3$ or $R_2$ and $R_4$ in *cis*-positions to each other are of a strongly pronounced and like electrical nature, because the energy of their repulsion would be considerable. Proceeding from such an assumption, it is easily understood why the addition, for example, of bromine to the anions of maleic and fumaric acids, results in the same substance—the

---

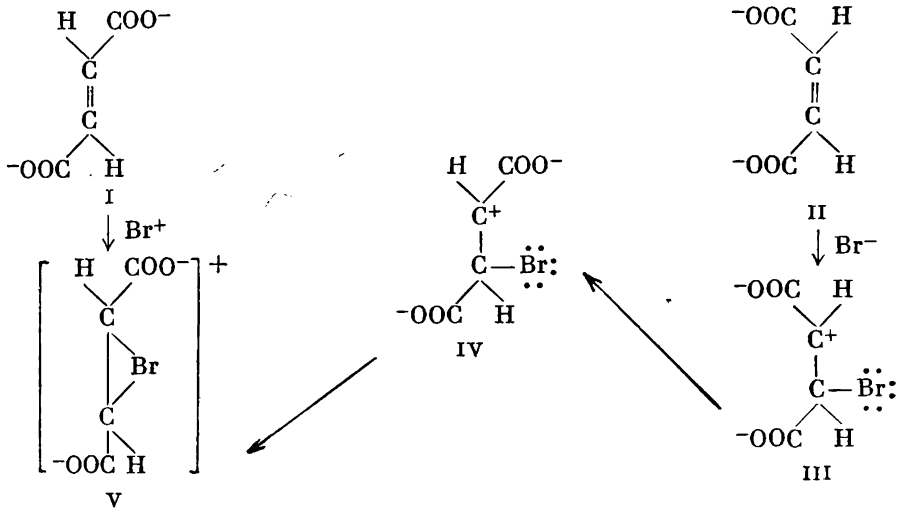
* See [15] for a different point of view.

** On the basis of the material presented above it may be deduced (independently of the facts of "mixed" additions) that the initial attack on the alkene is made by the halogen cation rather than anion. Had the halogen anion added initially,



then, not to mention the impossibility of formation of the three-membered onium ring, the presence of the electron pair at the carbon atom would ensure *cis*-addition. Such a hypothesis contradicts experimental findings.

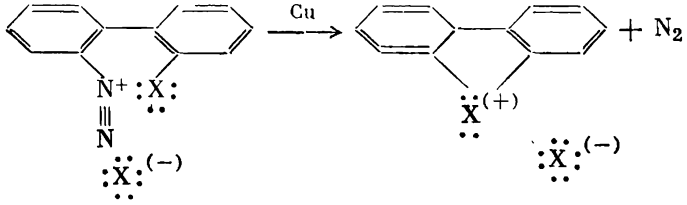
anion of meso-dibromosuccinic acid:



When the bromine cation is added to the anion of maleic acid (II) the three-membered onium ring cannot form in the initially appearing ion III because of the considerable repulsion of similarly charged carboxyl anions. The three-membered ring forms only after the carboxylic anions pass into the *trans*-position IV as a result of repulsion. The resulting ion V is identical with the ion formed independently from the anion of fumaric acid (I).

The above concepts of the mechanism of the bimolecular addition of halogens to alkenes satisfactorily explain presently known experimental facts.

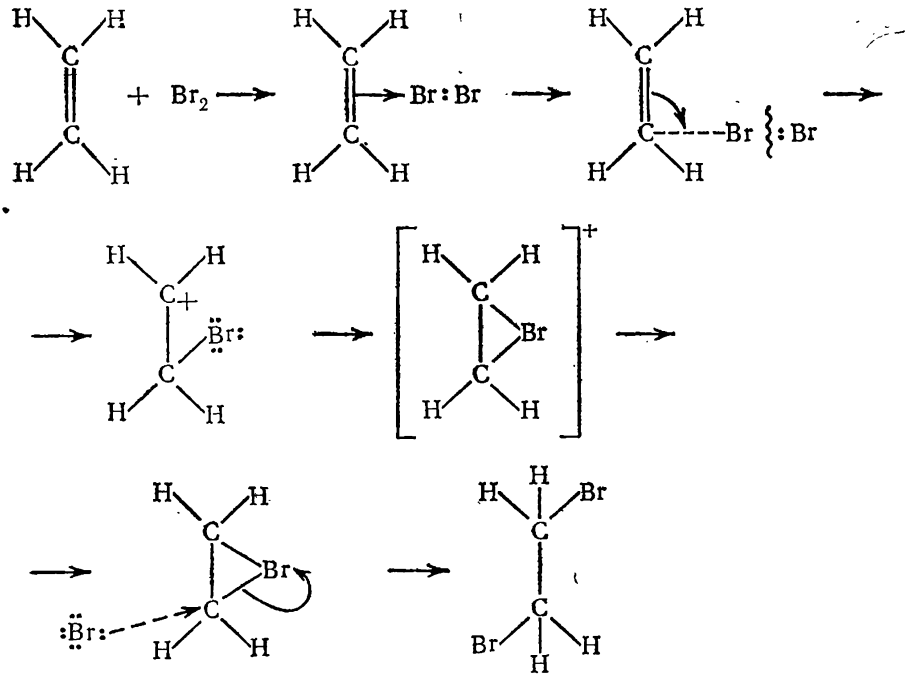
Until recently, an essential objection against the onium ring formation mechanism was that of all the halogens, onium compounds of the aromatic series were known only for iodine. However, recently stable bromonium and chloronium compounds were obtained from the following reaction [16]:



This greatly substantiated the hypothesis of the intermediate formation of three-membered onium rings during the addition of halogens to alkenes *.

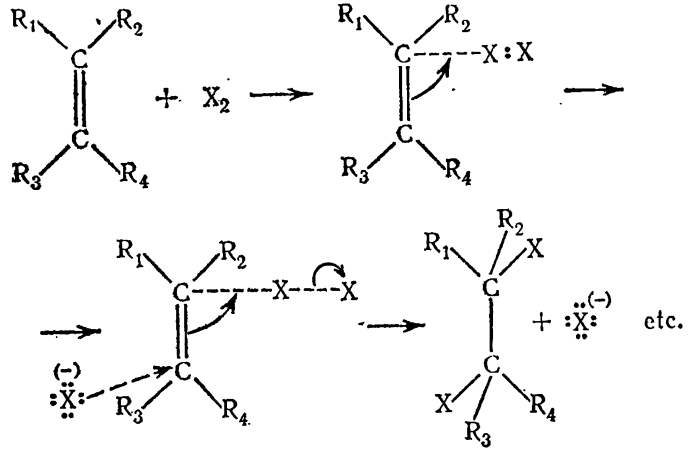
Thus, an outwardly simple reaction, for example, that of ethylene with bromine, actually takes the rather complex path:

* See [15] for a different point of view.



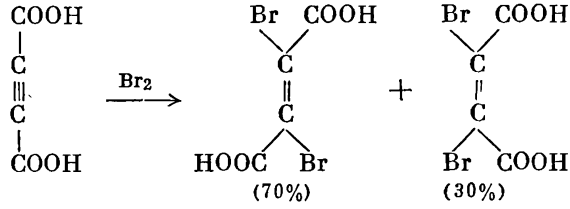
Under definite conditions (pages 214-215) the addition of bromine, iodine and chlorine to alkenes is a third-order reaction.

Such reactions proceed, probably, through an intermediate stage involving the formation of a complex compound ($\pi$-complex) of a halogen molecule with an alkene by inculcation of the $\pi$-electrons of the double bond in the deformed electron shell of the halogen molecule. Further attack on the $\pi$-complex by the halogen anion results in the final dihalogen derivative.

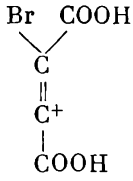


In these cases, apparently, no intermediate three-membered onium ring is formed.

The addition of halogens to acetylenic compounds is also predominantly a *trans*-addition. For example, the action of bromine on acetylenedicarboxylic acid in aqueous solution results in 70% dibromofumaric acid and 30% dibromomaleic acid.




In this case, evidently, the carbonium ion




is formed as an intermediate.

There is no reason to consider it possible for an intermediate cation with a three-membered onium ring to form during the addition of halogens to acetylenic compounds.

### Effect of Radicals Combined with Unsaturated Carbon Atoms on the Rate of Electrophilic Addition Reactions

The nature of the substituents $R_1$, $R_2$, $R_3$, $R_4$ in the compounds of the general type $R_1R_2C = CR_3R_4$ exerts a substantial influence on the reaction rate of electrophilic addition, for instance, on the rate of addition of halogens to the double bonds [17]. Substituents which activate the benzene ring with regard to electrophilic substitution reactions (page 489), also activate the carbon-carbon double bond. Conversely, substituents which deactivate the benzene ring also deactivate double bonds.

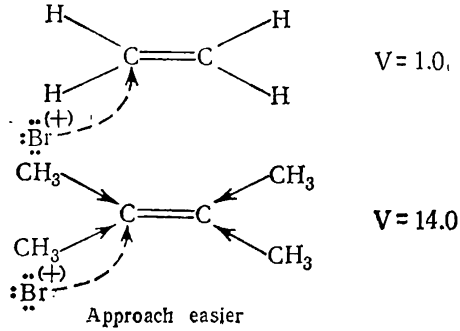
The relative rates of addition of bromine to various alkenes are given in Table 4-1.

TABLE 4-1

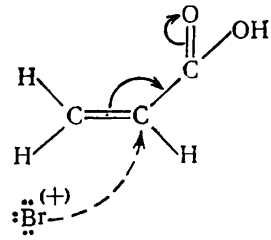
**Relative Rates of Addition of Bromine to Alkenes in $CH_2Cl_2$ Solution at —78°**

| | $V$ = relative rate |
|---|---|
| $CH_2=CH_2$ | 1.0 |
| $(CH_3)_2C=C(CH_3)_2$ | 14.0 |
| $(CH_3)_2C=CHCH_3$ | 10.4 |
| $(CH_3)_2C=CH_2$ | 5.53 |
| $C_6H_5CH=CH_2$ | 3.35 |
| $CH_3CH=CH_2$ | 2.03 |
| $CH_3CH=CHCOOH$ | 0.26 |
| $CH_2=CHBr$ | 0.04 |
| $CH_2=ClCOOH$ | 0.03 |

Such an order of change of the rates of addition of bromine, depending on the nature of the substituents at the unsaturated carbon atoms, is quite understandable. Since the first step of the reaction consists of the halogen cation attacking the alkene, it is obvious that approach of the cation $Br^+$ will become easier if the electron density of the double bond is increased. Conversely, a decrease in the electron density will make the first (slow) step of the reaction more difficult, and consequently will slow down the entire process of halogen addition. It is to be expected that such electron-repelling substituents as methyl groups will increase the electron density of the double bond and accelerate the addition reaction as compared with unsubstituted ethylene:

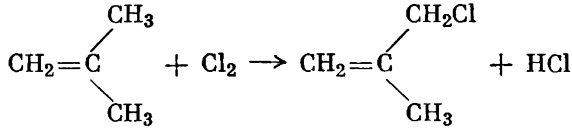



Conversely, such electron-acceptor groups as carboxyl lower the electron density of the carbon-carbon double bond, drawing it partly towards itself. As a result of this an attack by bromine on the unsaturated carbon atom should be more difficult than in unsubstituted ethylene.



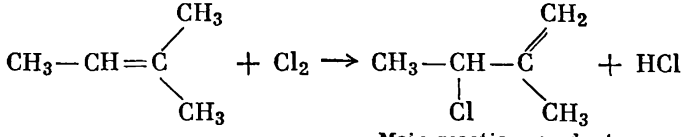

L'vov, Sheshukov and Kondakov showed [15] that in the reaction of chlorine with isobutylene, trimethylethylene and unsymmetrical methylethylethylene the expected dichlorides form only in small amounts. The main products are unsaturated monochlorides with the chlorine atom in the "allylic" position.

The assumption that such reaction products form as a result of direct substitution of α-hydrogen atoms (with respect to the double bond) without involving the double bond

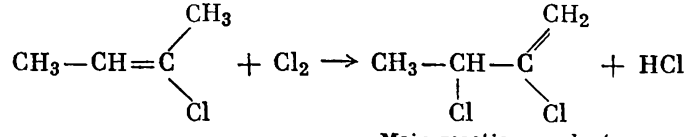



was disproved by Tishchenko [18].

This author established that the monochlorides are more reactive products and that they are formed through a shift of the double bond. This type of transformation takes place if there is a quaternary carbon atom at the double bond, for example:

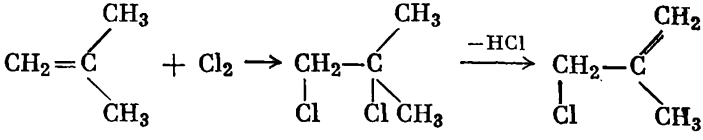



Main reaction product

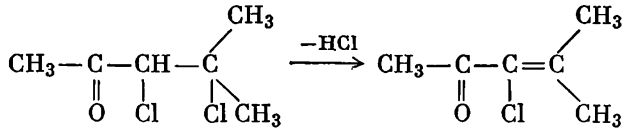



Main reaction product

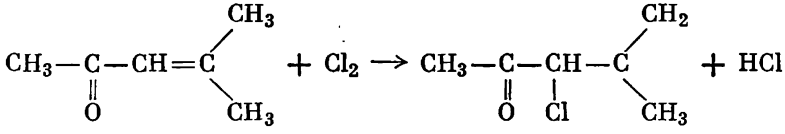
It may be assumed that the reaction proceeds through the stages of addition of the halogen molecule to the double bond followed by elimination of a molecule of hydrogen halide, for example:



However, as has been shown for the reaction of a halogen with mesityl oxide, such an assumption is incorrect, in the general case, at least, because the elimination of hydrogen chloride from mesityl oxide dichloride yields 3-chloro-2-methyl-pentene-2-one-4

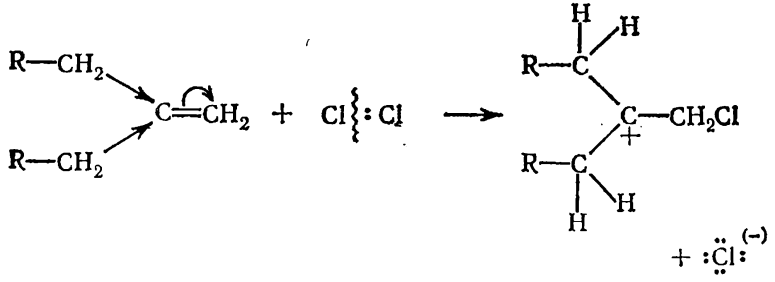


while the reaction of mesityl oxide with chlorine results in 3-chloro-2-methyl-pentene-1-one-4

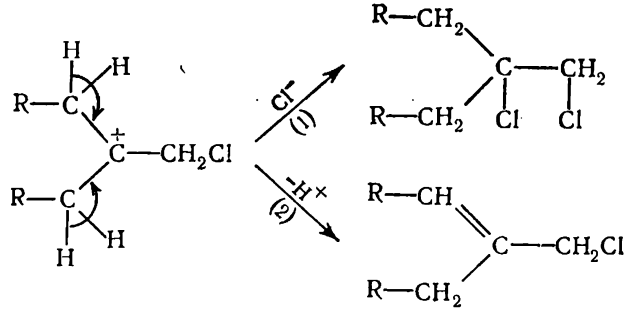


The mechanism of the above anomalous addition reactions may be explained as follows.

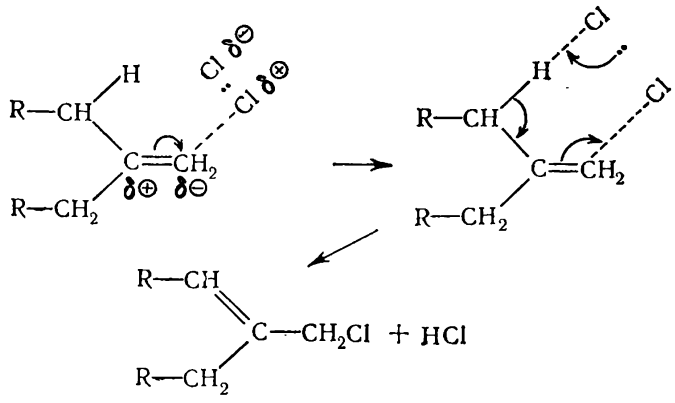
The first stage of the reaction consists, as usual, of addition of the halogen cation to the alkene. The direction of addition depends on the polarization of the double bond, which, in its turn, is determined by the influence of the neighbouring alkyl groups.



The cation formed may become stabilized either by the addition of a halogen anion or by the elimination of a proton:

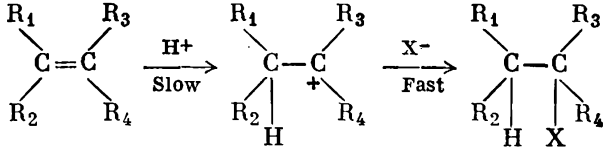


The ratio of the end products will probably depend on their stability, i.e., will be determined by thermodynamic factors. It is possible that the formation of a carbonium ion as a kinetically independent particle does not take place, and addition of the halogen cation and elimination of proton take place simultaneously:



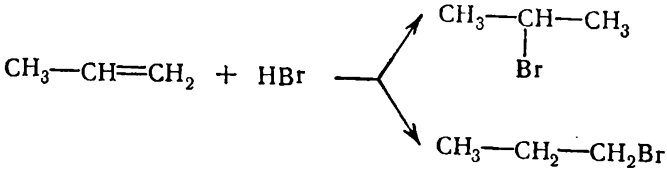

**Electrophilic Addition of Hydrogen Halides**

The addition of hydrogen halides to alkenes is an electrophilic reaction starting with the addition of a proton (page 213)




Obviously, the addition of hydrogen halides to symmetrical alkenes results in the formation of only one reaction product.

In the case of unsymmetrical alkenes, such as propylene, two directions of the reaction are possible

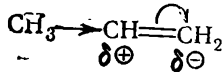



The order of addition of the elements of hydrogen halides to unsymmetrical alkenes is determined by Markovnikov's rule [19], according to which the hydrogen atom adds to the most hydrogenated, and the halogen atom, to the least hydrogenated carbon atom,

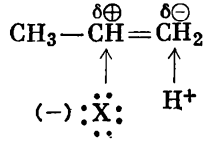
for example:

$$CH_3-CH=CH_2+HX \longrightarrow CH_3-CHX-CH_3$$

Markovnikov's rule is interpreted theoretically as follows: the double bond of the unsymmetrical alkene is polarized, as evidenced by the presence of a dipole moment in such compounds; for example, the dipole moment of propylene is 0.35 D. Obviously, the double bond is polarized by the action of, say, an electron-donor methyl group in the direction indicated by the curved arrow

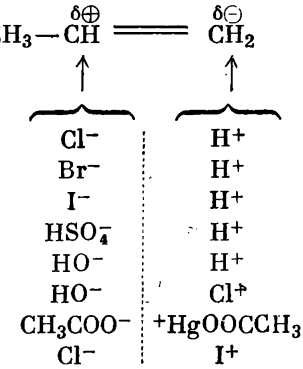


In the general case, this polarization determines the order of addition of the hydrogen halide elements



Thus, the *cation adding to the double bond attacks the more hydrogenated (negatively charged) carbon atom and the anion attacks the less hydrogenated (positively charged) carbon atom.*

Markovnikov's rule in its general form is obeyed by the ionic reactions of addition to alkenes of hydrogen halides, sulphuric acid, water, hypochlorous acid, mercury salts, and several other compounds:



| | |
|---|---|
| $Cl^-$ | $H^+$ |
| $Br^-$ | $H^+$ |
| $I^-$ | $H^+$ |
| $HSO_4^-$ | $H^+$ |
| $HO^-$ | $H^+$ |
| $HO^-$ | $Cl^+$ |
| $CH_3COO^-$ | $^+HgOOCCH_3$ |
| $Cl^-$ | $I^+$ |

It can be seen that in the case of addition reactions to alkenes only static factors (structure of the initial alkene molecule and of the reagent) were considered for the explanation of Markovnikov's rule.

A different independent approach can be used to explain Markovnikov's rule, by examining dynamic factors (structure of the activated complex, of the transition state).

It is known that the addition of hydrogen halides to the carbon-carbon double bond is a two-stage electrophilic reaction, starting with the addition of a proton, e.g.,

$$CH_3-CH=CH_2 \xrightarrow[\text{Slow}]{H^+} CH_3-\overset{+}{C}H-CH_3 \xrightarrow[\text{Fast}]{} CH_3-\underset{\displaystyle X}{\underset{|}{CH}}-CH_3$$

Of the two cations which may form as a result of the addition of a proton to propylene, the isopropyl cation and the *n*-propyl cation, the former is more stable. And it is the one that actually forms.

Thus, consideration of dynamic factors results in an independent explanation of Markovnikov's rule: *reactions of addition to double bonds proceed in the direction of formation of the most stable intermediate cation.*

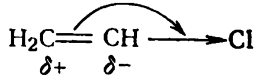
It is quite apparent that in the reactions of addition to alkenes examined above, static and dynamic factors act in agreement, favouring a single direction of the reaction. It is difficult to decide here which is the decisive factor.

If we pass over to chlorosubstituted ethylenes, it becomes clear that in this case the dynamic factor is the decisive one.

The addition of hydrogen bromide to vinyl chloride procceds according to Markovnikov's rule

$$H_2C=CH-Cl+H-Br \longrightarrow CH_3-CHBr-Cl$$

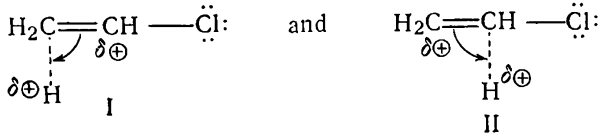
while in the nonreacting molecule of vinyl chloride the negative end of the dipole is chlorine and the double bond is polarized (beyond doubt) in such a way that the most hydrogenated carbon atom bears a certain positive charge:



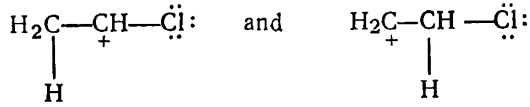

It is evident that in the reaction between vinyl chloride and HBr the static factor (the nature of polarization of the double bond under the influence of the chlorine atom) favours addition of hydrogen bromide contrary to Markovnikov's rule.

To be able to judge the dynamic factors of this reaction, it is necessary to examine the two transition states, I and II, or the two

cations Ia and IIa, formed through these transition states, respectively:



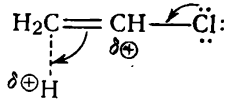

I II




Ia IIa

Transition state I arises when the vinyl chloride molecule is attacked by a proton in accordance with Markovnikov's rule, and transition state II sets in when the attack contradicts Markovnikov's rule. In both cases a positive charge forms on the carbon atom (increasing with the degree of approach of the proton to the vinyl chloride molecule), and this increases the energy of the system.

However, in transition state I the positive charge which forms may be partly compensated by a shift of the outer electron cloud of the chlorine atom.



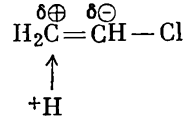
As a result, the positive charge is not localized on the carbon atom (the chlorine atom also becomes positively charged to a certain extent), and that is why the energy of the system decreases.

In transition state II, owing to its structural peculiarities, the positive charge forming on the carbon atom of the methylene group cannot be even partly compensated by a shift of the electron cloud to the chlorine atom, because the latter is too far away. The presence of a localized positive charge on the carbon atom is responsible for the considerable energy of the system.

Thus, the energy of transition state I is smaller than that of state II, and therefore the reaction in question proceeds according to Markovnikov's rule (through transition state I with the lower activation energy) in spite of the fact that the polarization of the initial molecule (static factor) favours the reverse reaction.

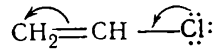
The intermediate cation will be cation Ia which is more stable than cation IIa.

However, the static factor, comprising unfavourable polarization of the molecule for HBr addition according to Markovnikov's rule, is reflected in the reaction rate. As the proton will have greater difficulty in approaching a carbon atom which carries a certain positive charge



the rate of addition of HBr to vinyl chloride is many times slower than to unsubstituted ethylene.

Often the electronic-structural formula of vinyl chloride is represented as follows:

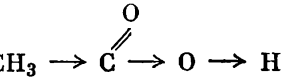


Apparently, this formula is favoured because of the seeming possibility of easily explaining the addition of hydrogen halides according to Markovnikov's rule.

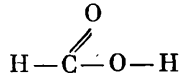
However, examination shows this formula to be incorrect.

Straight arrows are used to indicate relative but not absolute electron displacements.

For example, in the formula

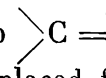


the straight arrow between oxygen and hydrogen does not mean that the electron pair linking the oxygen with the hydrogen (O : H), is located closer to the hydrogen than to the oxygen. This arrow indicates that the density of the electron cloud of the pair in question (the centre of which is located closer to the oxygen) is shifted somewhat toward hydrogen, *relative to the situation in the formic acid molecule*

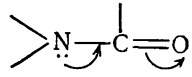


As pointed out earlier (page 53), the scale of inductive effects of atoms and groups of atoms is based on comparison with hydrogen.

Bent arrows are used to indicate both relative and absolute electron displacements.

In the formula of the carbonyl group  the bent arrow indicates that the π-electron pair is displaced from the centre of the

carbon-oxygen bond toward the oxygen (absolute displacement). In the formula of the amide group the bent arrow on the left indicates that the free electron pair is not fully located on the nitrogen atom, but is displaced (absolutely) towards the carbon atom:



In representing transition states bent arrows also indicate absolute rather than relative electron displacements.

However, bent arrows are sometimes used for representing relative displacements, which is also quite natural.

But if in such cases it is forgotten that the displacements indicated are *relative* and these relative displacements are taken for absolute displacements, misunderstandings result.

Here is an example.

In considering chlorine derivatives of alkanes and alkenes it is evident that the chlorine atom forms the negative end of the bond:

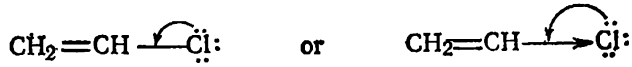
$$R_1R_2R_3C—Cl \text{ and } CH_2=CH—Cl$$

or

$$R_1R_2R_3C \longrightarrow Cl \text{ and } CH_2=CH \longrightarrow Cl$$

However, when the two compounds are compared certain differences between their C — Cl bonds become apparent. The C — Cl bond in vinyl chloride is stronger (probably because of greater electron density), and the dipole moment of vinyl chloride is smaller than that of alkyl chlorides.

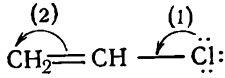
If the increase in the electron density of the C — Cl bond in the unreacting molecule of vinyl chloride were due to the free electrons of the chlorine atom, it would be quite proper to represent vinyl chloride as



This formula would indicate that although the centre of the electron cloud of the C — Cl bond is closer to the chlorine atom, it is not as close as in alkyl chloride molecules.

However, a further step is made which is not legitimate though the bent arrow from the chlorine atom to the carbon has a relative meaning (comparison to the chlorine atom in alkyl chlorides) and the centre of electron density of the C — Cl bond is actually displaced towards the chlorine atom (which is the negative end of the

molecule): a second bent arrow is drawn

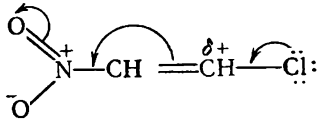


and this gives the false impression that the C = C bond is so polarized that the carbon of the methylene group carries a partial negative charge.

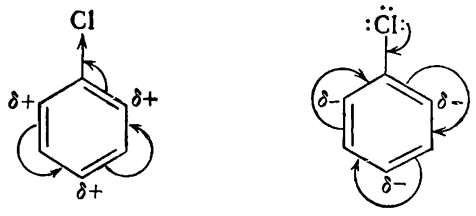
This second arrow reflects neither an absolute nor a relative (in comparison, say, with the ethylene molecule) electronic displacement.

Hence, this formula of vinyl chloride is incorrect.

The conjugation, indicated by both bent arrows, may become real however if one of the atoms of the methylene group is replaced by a strongly electron-attracting group, e.g.:



A quite similar problem is encountered in examining the structural-electronic formula of chlorobenzene (see page 491). The structure of chlorobenzene should be represented by formula (I) and not by formula (II).

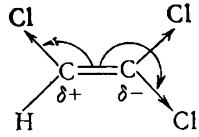


I II

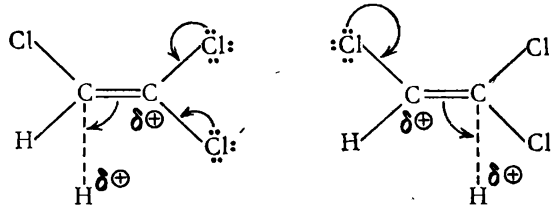
The direction of the reaction of addition of hydrogen bromide to trichloroethylene can be explained in a similar way:

$$CCl_2{=}CHCl + HBr \longrightarrow CCl_2Br{-}CH_2Cl$$

The nature of polarization of the double bond under the influence of chlorine atoms favours hydrogen bromide addition (as is the case with vinyl chloride) contrary to Markovnikov's rule.

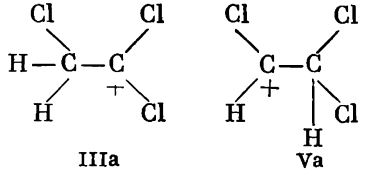


However, of the two transition states:



III IV

the energy of state III is smaller because the electrons of two chlorine atoms participate in neutralizing the positive charge on the carbon atom while in state IV only those of one chlorine atom participate. Consequently of the two possible intermediate cations



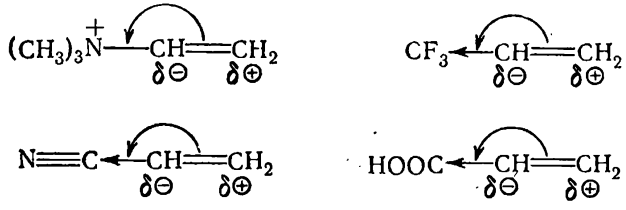
IIIa Va

IIIa is more stable. This fact determines the direction of the reaction, which follows Markovnikov's rule. However, unfavourable polarization of the double bond of trichloroethylene and the low electron density of the double bond exert such an influence on the rate of the reaction that it can proceed only in the presence of catalysts (such as ferric chloride).

When groups possessing strong electron attraction are linked to unsaturated carbon atoms, the elements of hydrogen halide add in the reverse order, so that the hydrogen adds to the less, and the halogen to the more hydrogenated carbon atom, e.g.:*

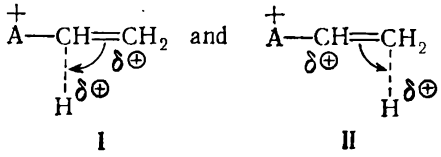
$$(CH_3)_3\overset{+}{N}-CH=CH_2+HI \longrightarrow (CH_3)_3\overset{+}{N}-CH_2-CH_2I$$
$$CF_3-CH=CH_2+HBr \longrightarrow CF_3-CH_2-CH_2Br$$
$$N\equiv C-CH=CH_2+HBr \longrightarrow N\equiv C-CH_2-CH_2Br$$
$$HOOC-CH=CH_2+HBr \longrightarrow HOOC-CH_2-CH_2Br$$

In all these cases the nature of polarization of the double bond under the influence of the neighbouring electron-attracting group favours addition of a proton to the less hydrogenated carbon atom.



* See page 272 concerning radical addition of hydrogen halides to alkenes.

Both possible transition states in all these cases can be illustrated as follows (A = atom carrying a positive or a partial positive charge):

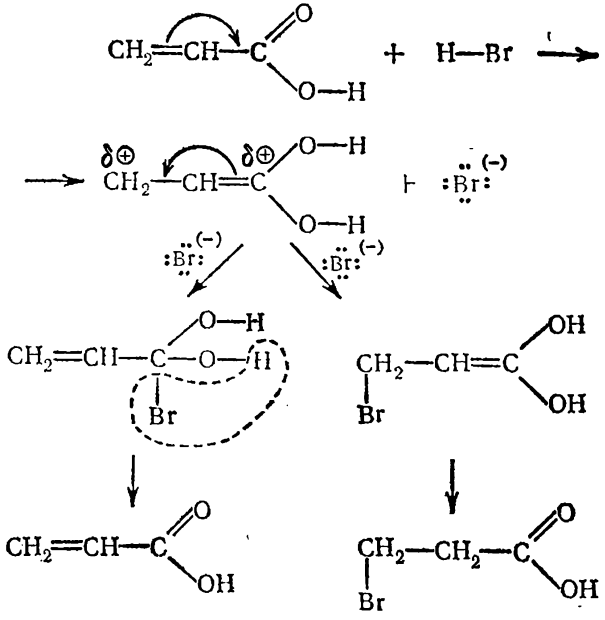


I II

The energy of states II is higher than the energy of states I because of repulsion of the two positively charged and interlinked atoms C and A.

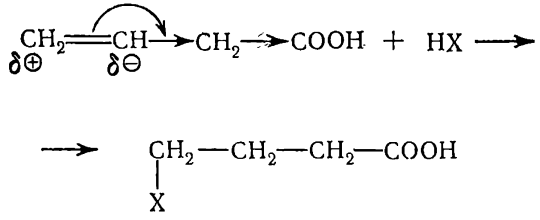
Thus, in the cases examined the static and dynamic factors favour the direction of the addition reaction in which the proton adds to the less hydrogenated carbon atom.

The "abnormal" addition of hydrogen halides to unsaturated acids or their nitriles can be explained by the fact that the reaction probably proceeds as a 1,4-addition, as shown in the following scheme:



It is interesting that the carboxyl group causes the "abnormal" addition of hydrogen halides to the double bond even when it is not conjugated with the latter, as in the case of vinylacetic acid. Since there are no conjugated bonds in this case, addition obviously takes

place in the 1,2-position.



If the carboxyl group is sufficiently far away from the double bond, the addition of hydrogen halides follows Markovnikov's rule. In this case the influence of the hydrocarbon part of the molecule (possessing electron-donor properties) prevails over the electron-attracting effect of the carboxyl group, which diminishes rather rapidly down the chain

$$CH_2{=}CH{-}CH_2{-}CH_2{-}CH_2{-}COOH + HX \longrightarrow$$
$$\longrightarrow CH_3{-}\underset{\displaystyle X}{\underset{|}{CH}}{-}CH_2{-}CH_2{-}CH_2{-}COOH$$

On the basis of this discussion the most general formulation of Markovnikov's rule would be: "*Addition of the elements of hydrogen halides (and of certain other substances) to unsaturated compounds takes place in such a way that the most stable of all possible cations are formed as intermediates.*"

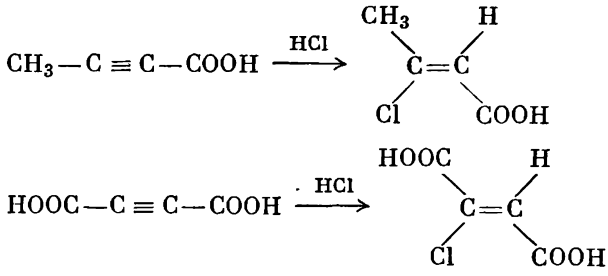
This general formulation also embraces cases of addition of hydrogen halides to unsaturated hydrocarbons whose unsaturated carbon atoms are linked with strong electron-acceptor groups. These cases were previously considered abnormal.

### Kinetics and Stereochemistry of Addition Reactions of Hydrogen Halides to Miltiple Carbon-Carbon Bonds

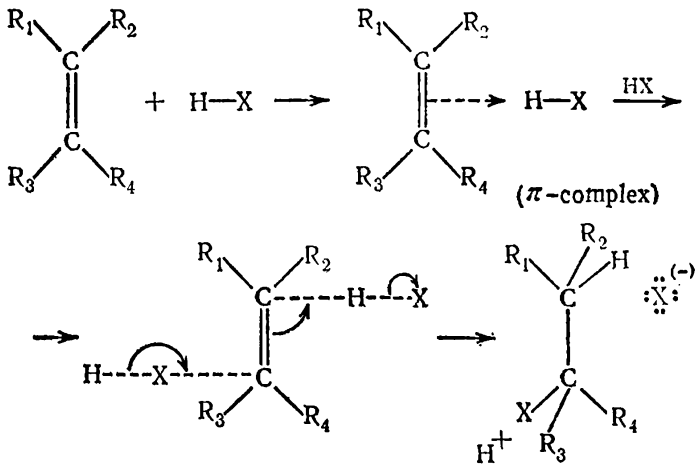
The study of the kinetics of addition reactions of hydrogen halides to ethylenic or acetylenic compounds shows that these reactions are not simple bimolecular processes (one molecule of an unsaturated compound reacting with one molecule of hydrogen halide), but involve a third molecule (hydrogen halide molecule). This conclusion is borne out by the fact that the rate of addition reactions depends more on the concentration of the hydrogen halides than on the concentration of the unsaturated compound.

Reactions of HX with unsaturated compounds are *trans*-additions; the most reliable data on the spatial direction of addition (stereoche-

mistry) were obtained for the addition of hydrogen halides to acetylene compounds:



The addition of hydrogen halides to alkenes evidently proceeds through the stage of an alkene-hydrogen halide complex due to a hydrogen bond ($\pi$-complex).* The complex reacts with a second molecule of hydrogen halide yielding the end product:



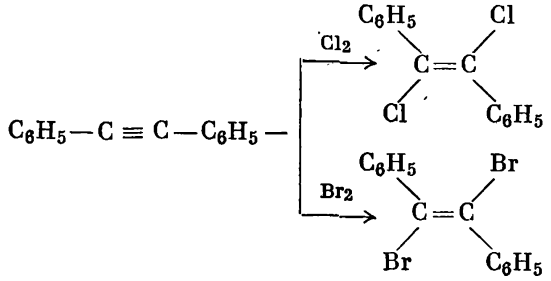

**Stereochemistry of Addition Reactions to the Triple Carbon-Carbon Bond**

The stereochemistry of addition of halides to the C ≡ C bond has been studied insufficiently.

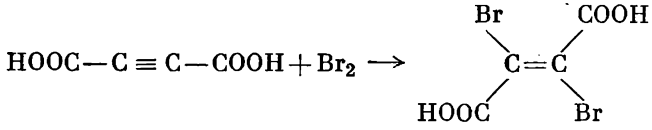
The addition of chlorine or bromine to tolane results mainly

* Being bases in a sense, alkenes do possess proton affinity. This is evident, for instance, from the fact that, unlike saturated hydrocarbons, alkenes are soluble in liquid hydrogen fluoride.

in *trans*-dichlorostilbene and *trans*-dibromostilbene, respectively [20].



Similarly, when bromine is added to acetylenedicarboxylic acid, the resultant is predominantly dibromofumaric acid:



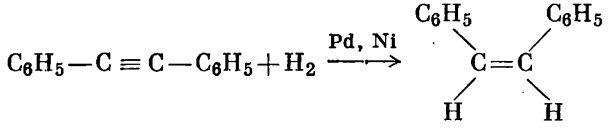
In all the cases indicated the addition to the triple bond is predominantly a *trans*-addition.

However, owing to the small number of cases studied it would be imprudent to maintain that halogens add to the C ≡ C bond in *trans*-positions as a rule. Moreover, it is definitely known that the stereochemistry of addition to acetylene compounds may depend on the experimental conditions.

The addition of hydrogen to acetylene compounds has been studied somewhat more thoroughly with respect to stereochemistry [21] than halogen addition.

If elementary hydrogen adds to acetylenic compounds in the presence of platinum, palladium or nickel as catalysts, *cis*-addition is generally observed*.

Thus, when tolane is hydrogenated over palladium or nickel [23] the result is *cis*-stilbene with only insignificant amounts of *trans*-stilbene.



*Cis*-addition in this case can be explained by the fact that the organic molecule is adsorbed on the catalyst surface, and both hydro-

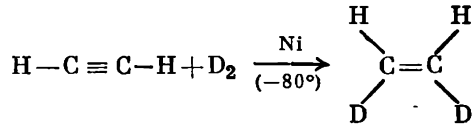
* Several investigations [see 22] describe the formation of *trans*-alkenes together with the *cis*-alkenes. The ratio of *cis*- to *trans*-alkenes depends on the reaction conditions.

gen atoms participating in the addition approach the triple bond simultaneously (probably as a hydrogen molecule).

Another explanation may be that the adsorbed molecule in the first stage of reaction is linked with one hydrogen atom and with a metal atom of the catalyst surface simultaneously. In the next stage of the reaction the metal atom is replaced by a second hydrogen atom in such a way that the two hydrogen atoms in the resulting alkene are on the same side of the double bond [24].

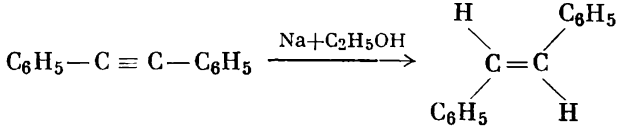
This stereochemical result is doubtlessly a consequence of the reaction itself rather than of a secondary *trans-cis*-transformation, because *trans*-alkenes are more stable than *cis*-alkenes.

Confirmation of *cis*-addition in the above reaction was obtained n the addition of deuterium ($D_2$) to acetylene over a nickel catalyst.

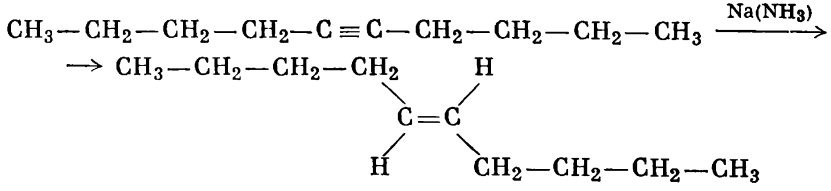


The reaction resulted predominantly in *cis*-deuteroethylene (there is no substantial difference between the stability of *cis*- and *trans*-deuteroethylenes).

When acetylenic compounds are reduced by "metal + acid" or other chemical substances of a reducing nature, *trans*-addition is observed. For example, the reduction of tolane by sodium in ethanol results in *trans*-stilbene:



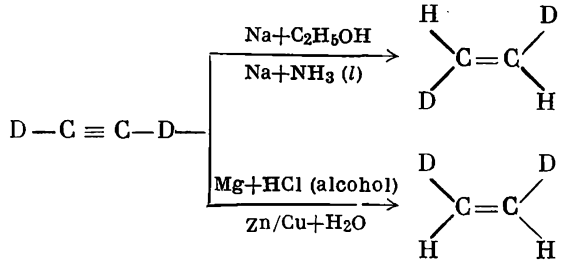
The reduction of decine-5 with sodium in liquid ammonia yields *trans*-decene-5



However, the *trans*-addition of hydrogen in the above reactions cannot be regarded as a general rule.

Reduction of deuteroacetylene with sodium in alcohol or with sodium in liquid ammonia results in *trans*-deuteroethylene, while

reduction with magnesium in alcoholic hydrogen chloride or with Zn — Cu alloy in water yields *cis*-deuteroethylene [25].




If there is no way of explaining the formation of the *trans*-product, the formation of the *cis*-product can be attributed to the fact that the reduction of acetylene by magnesium in alcoholic hydrogen chloride or by zinc-copper alloy in water is not a chemical reduction but catalytic hydrogenation on a metal surface, which, as it was indicated above, is a *cis*-addition of hydrogen.

The stereochemistry and kinetics of the addition of hydrogen compounds were studied thoroughly by Shilov and Smirnov-Zamkov using dimethyl acetylenedicarboxylate as an example [26].

These workers hold that the steric direction of addition is determined by the formation of a transient complex at the moment of the reaction.

In glacial acetic acid, hexane, nitromethane, and without a solvent, the reaction yields approximately an equimolecular mixture of bromomaleic and bromofumaric esters. In benzene more than 90% of the product is the *trans*-isomer. Concentration, temperature, addition of peroxides or antioxidants have no substantial effect on the course of the reaction. Addition of LiBr or $HgBr_2$ increases the yield of the *trans*-product.

The rate of addition reaction obeys the third-order equation

$$-\frac{d[HBr]}{dt} = kA[HBr]^2,$$

$A$ being the concentration of the acetylenedicarboxylate.

In the presence of lithium bromide the reaction rate increases (Fig. 4-1), and the hydrogen bromide concentration becomes first-power in the kinetic equation. Kinetic data are adequately described by the equation

$$-\frac{d[HBr]}{dt} = k'A[HBr][Br^-]$$

The rate of addition of hydrogen bromide to dimethyl acetylenedicarboxylate depends greatly on the solvent:

in $CH_3COOH$ $K^{20}=0.21$
in $C_6H_6$ $K^{20}=1.86$
in $C_6H_{14}$ $K^{0}=5,200$

The effect of solvents and additives on the rate of addition of HBr to $CH_3OOC - C \equiv C - COOCH_3$ is illustrated in Fig. 4-1.

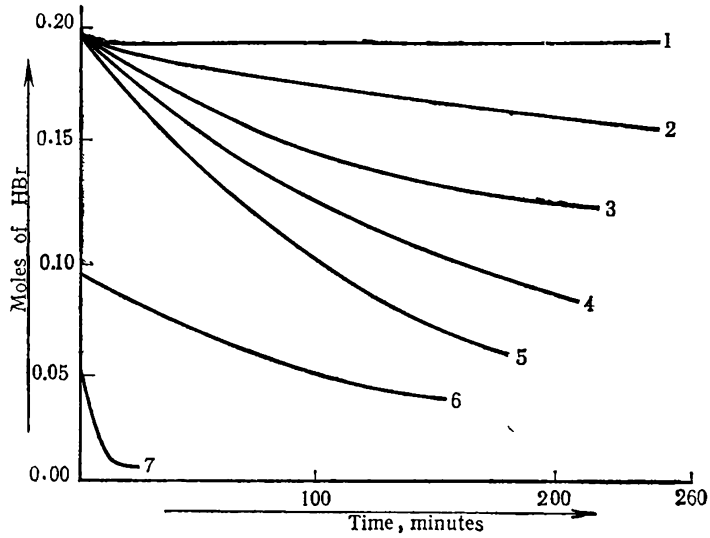
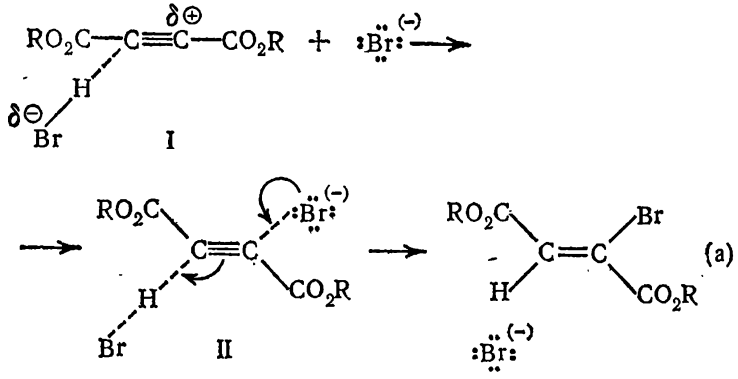



FIGURE 4-1 Effect of solvents and additives on the rate of addition of hydrogen bromide to dimethyl acetylenedicarboxylate

Solvents: *1-5*—anhydrous acetic acid; *6*—benzene; *7*—hexane. Additives: *1*—acetic anhydride (0.5*M*); *2*—water (2*M*); *4*—water (0.1*M*); *5*—lithium bromide (0.16*M*); *3* and *7*—no additives. Temperature: *1-6*—20°C; *7*—0°C

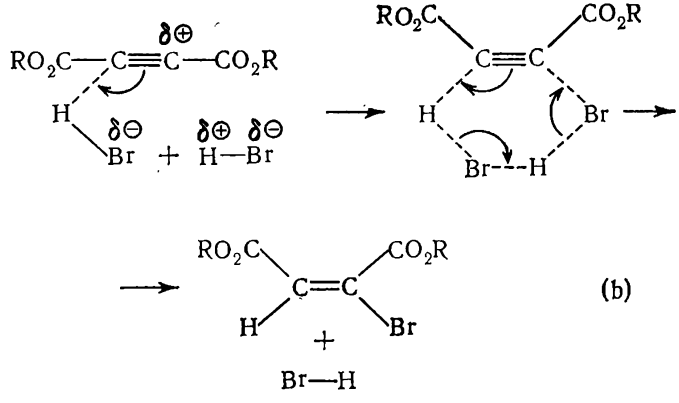
The results of the experiments were explained as follows: the reaction takes place in two stages. First a complex compound ($\pi$-complex) of the unsaturated ester with HBr is formed. The complex then reacts (second stage) with another molecule of HBr or with a bromine anion. The first stage determines the concentration of the complex in solution, the order and overall reaction rate depending on the second (slower) stage. The electric charges in the initial complex are evidently distributed in the presence of $Br^-$ approximately as represented by formula I of scheme (a). The negatively charged groups, for example, $Br^-$, will naturally tend to approach the positive carbon atom from the side farthest away from $Br^{\delta\ominus}$,

that is, in the *trans*-position (II)



The HBr molecule may react with the complex I in the same way as $Br^-$, but probably, less vigorously, because the bond between bromine and proton counteracts the formation of an active complex.

On the other hand, the HBr molecule has a positive centre, HBr is capable of approaching the negative end of complex I resulting in *cis*-addition:

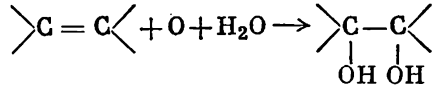


The effect of the nature of the solvent and of additives is probably due to their ability to form complexes with HBr. A more stable bond with HBr results in a decrease in concentration of complex I, slowing down the reaction.

Thus, the stereochemical direction of the reaction depends on the structure of the active complex, which is determined by the structure of the reactants and the conditions of the reaction.

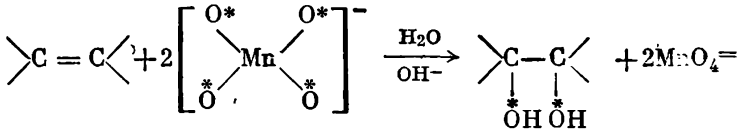
### Oxidation of Alkenes with Permanganate (Wagner Reaction)

The reaction with permanganate, characteristic of alkenes [27], takes place at a high pH with the formation of α-glycols as the main product:

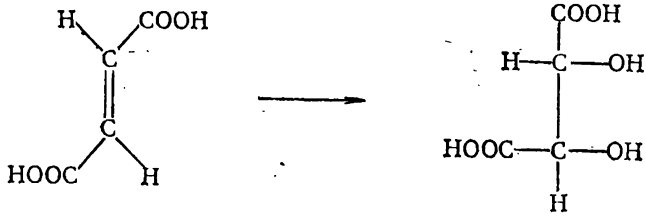


According to this simplified scheme, two oxygen atoms, one from the permanganate and the other from the solvent, are transferred to the molecule of the glycol formed.

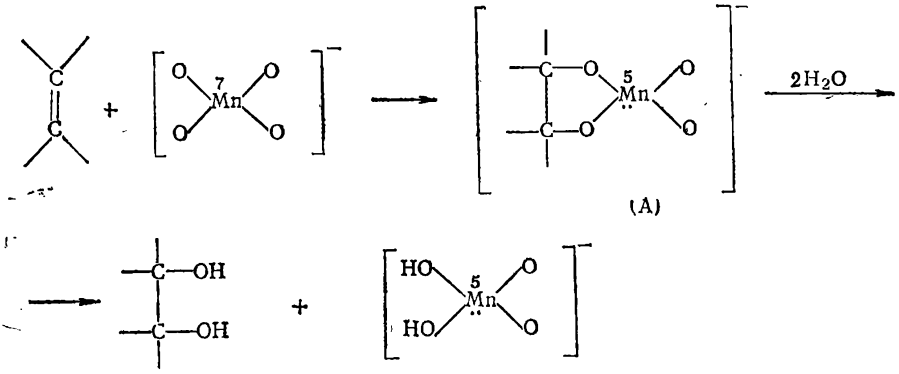
However, recent investigations [28] of the Wagner reaction using $MnO_4^-$ labeled with $O^{18}$ show that in reality both oxygen atoms in the glycol molecule owe their origin to the permanganate.



The stereochemical course of the Wagner reaction is such that hydroxyl groups take *cis*-positions [29], e.g., in the case of cyclohexane or maleic and fumaric acids:



To explain the course of the Wagner reaction as a *cis*-addition a mechanism involving the formation of an intermediate cyclic complex (A) was proposed:




and then:

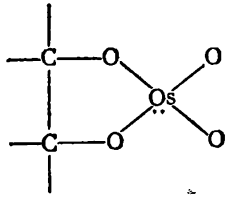
$$H_2MnO_4^- + MnO_4^- + 2OH^- \xrightarrow{\text{Fast}} 2MnO_4^{=} + 2H_2O$$

According to the above mechanism, the formation of the intermediate complex (A) involves transfer of an electron pair from the alkene to manganese through oxygen.

Although the $Mn^{5+}$ state is relatively uncommon for manganese, $H_2MnO_4^-$ is stable in the cold in 8-10 *N* sodium hydroxide solution [30]. In a solution of lower basicity it should react with $MnO_4^-$ to form the $MnO_4^{=}$ ion. The latter also oxidizes the alkene to *cis*-α-glycol, but much slower than $MnO_4^-$.

It should be noted that there are no experimental proofs so far that the cyclic complex (A) actually forms in the Wagner reaction.

However, an analogous cyclic osmium ester



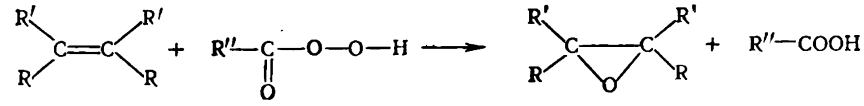
was isolated [31] from the reaction mixture formed on oxidation of alkenes with osmium tetroxide $OsO_4$ into α-glycols.

This oxidation is also a *cis*-addition and its mechanism is evidently similar to that of the Wagner reaction.

It should be noted that the question of the Wagner reaction mechanism is very complex, because this mechanism apparently depends on many factors: structure of the alkene, acidity of the solution, reaction temperature*.

### Oxidation of Alkenes with Peracids (Prilezhaev Reaction)

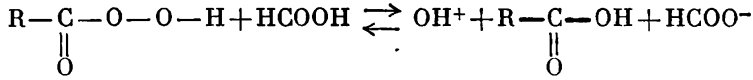
Prilezhaev discovered and investigated the reaction of oxidation of alkenes with peracids, resulting in the addition of oxygen to alkenes to form α-oxides [34].



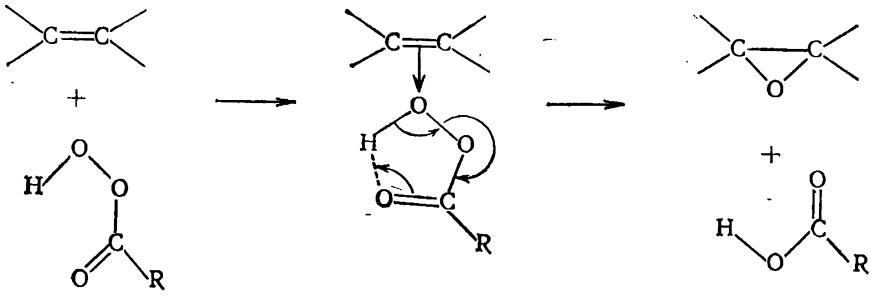
cis

This is a reaction of *cis*-addition of oxygen. The alkyl substituents R and R′ facilitate this reaction, which is an indication of the electrophilic nature of the attack on the double bond in this reaction.

In polar solvents, e.g., in formic or acetic acid, the attacking reagent is evidently hydroxonium ion $OH^+$, formed as a result of the following equilibrium:



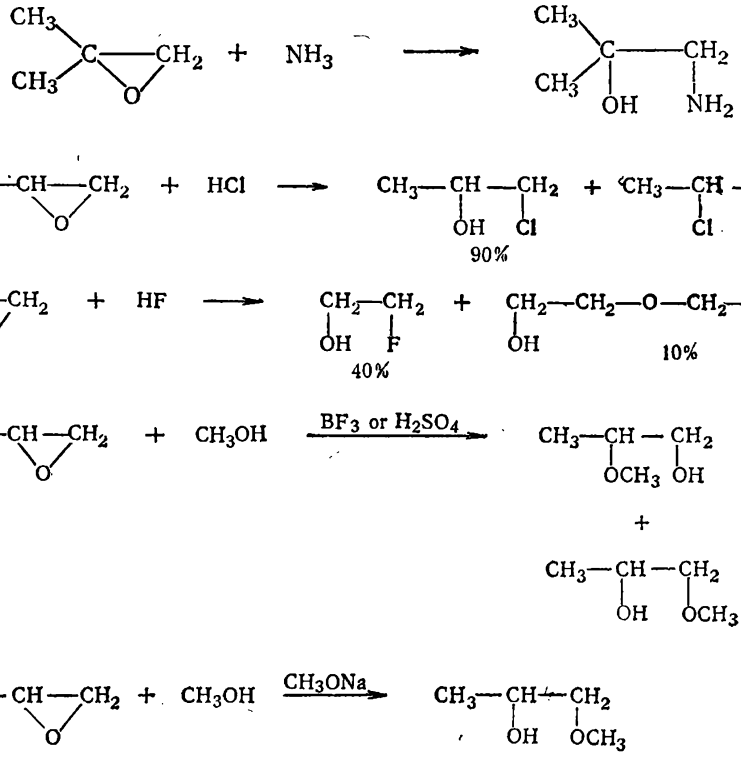
In nonpolar solvents the reaction apparently passes through the stage of formation of a π-complex of the alkene with the peracid involving the following bond redistribution [35]:



* For details see [32, 33].

### Addition Reactions to α-Oxides

The α-oxides of the alkane series can add substances of a basic nature such as ammonia and amines [36-39], acidic substances such as hydrogen halides [40-44] and neutral substances such as water or alcohols in the presence of acid or alkaline catalysts [45]:




It should be noted that the above reactions of epoxides are simultaneously reactions of addition to a three-membered ring and substitution reactions at the saturated carbon atom.

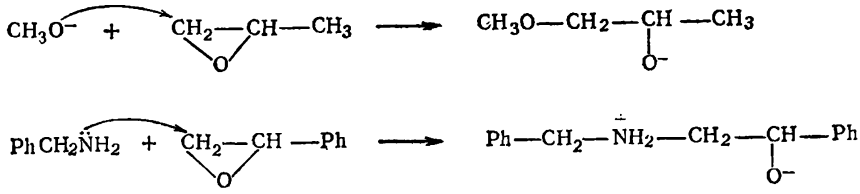
One of the specific features of α-oxides is the presence of considerable Baeyer strain in their molecules; consequently their C — O bond is incomparably easier to break than those of ether molecules.

The question of orientation in these reactions is rather complicated [46].

It is difficult to judge of the mechanism owing to the lack of experimental data on the kinetics and stereochemistry of epoxide reactions.

It is possible that the mechanism of ring opening of epoxides may differ depending on the nature of the reagent and reaction conditions.

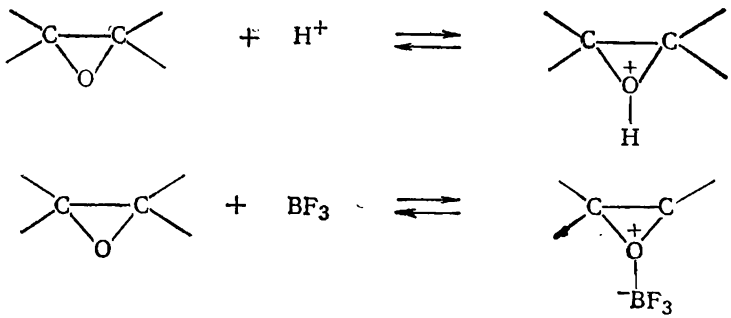
Thus, epoxide reactions with nucleophilic reagents are evidently bimolecular and their course is determined by factors analogous to $S_N2$ reactions.



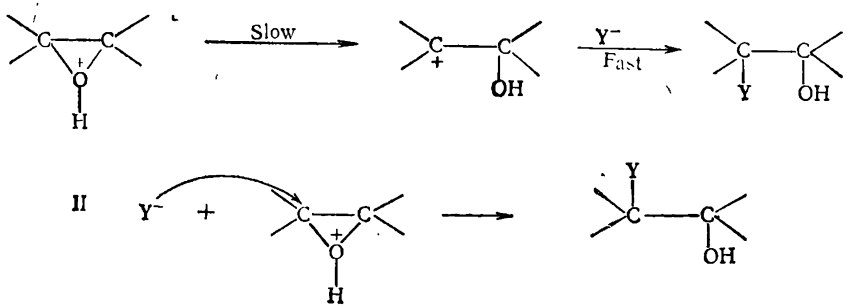
As is known (Chap. 2), bimolecular nucleophilic substitutions are promoted by highly nucleophilic reagents and by the absence of alkyl substituents at the carbon atom at which the substitution occurs.*

Therefore, it is not surprising that if one of the carbon atoms of the ethylene oxide ring is less replaced by alkyl groups than the other, the reagent will attack predominantly, and sometimes exclusively, the less substituted atom.

In reactions with acidic reagents or with neutral substances in the presence of acid catalysts an oxonium compound forms first:



The subsequent stage of opening of the three-membered rings of onium compounds may be monomolecular or bimolecular.



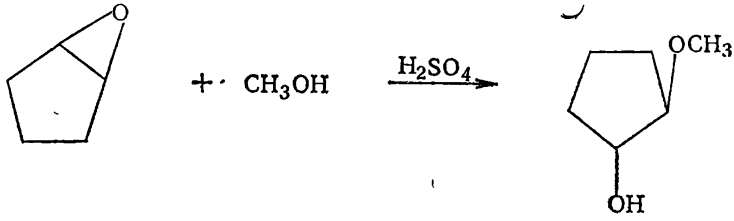
* For example, the conditions for bimolecular hydrolysis are the most favourable for $CH_3$—Cl and the least favourable for $(CH_3)_3C$—Cl.

Kinetic investigations of the reaction of ethylene oxide with hydrogen chloride favour the second mechanism. This reaction obeys the equation of third-order reactions:

$$V = K_3\,[\text{ethylene oxide}]\,[H^+][X^-]$$

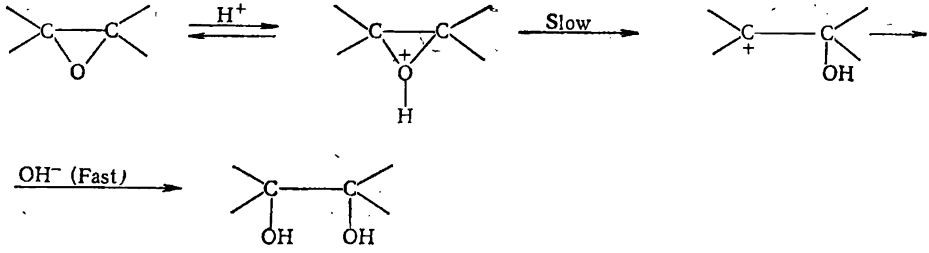
Stereochemical evidence also favours this mechanism: many ring-opening reactions of oxides involve complete inversion of configaration.

Consider, for example, the addition of methanol to cyclopentene oxide in the presence of sulphuric acid; the result of this reaction is exclusively *trans*-2-methoxycyclopentanol [47].

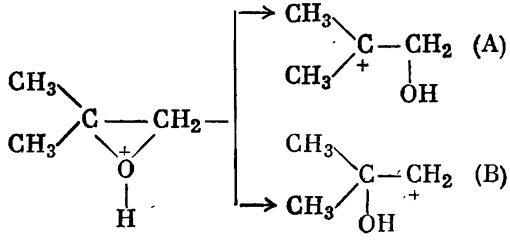



If the reaction passed through the stage of formation of an intermediate carbonium ion, both the *cis*- and *trans*-isomers might have been expected to result.

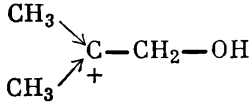
On the other hand, independent data [48] indicate that the hydrolysis of oxides, catalyzed by acids, proceeds through the carbonium ion stage according to the monomolecular mechanism:




If the reacting oxide is unsymmetrical, rupture of both C — O bonds is formally possible resulting in two different carbonium ions, for example:



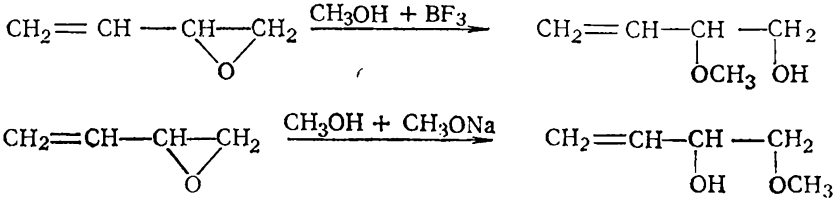
It can easily be perceived, however, that the cations A and B have different stabilities. Owing to the inductive effect of the alkyl groups, cation A is more stable and therefore it would be the one to form predominantly



Thus, in monomolecular reactions of the type of oxide hydrolysis in the presence of acids, the oxygen-carbon bond breaks at the most substituted carbon atom.

It follows from the above discussion that an unsymmetrical α-oxide may yield different products with the same nucleophilic reagent in the presence or absence of acid catalysts because of different reaction mechanisms.

Probably, the addition of methanol to divinyl monoxide in the presence of $BF_3$, observed by Petrov, [46], is a monomolecular reaction (passing through the carbonium ion stage), while in the presence of an alcoholate it is a bimolecular reaction:

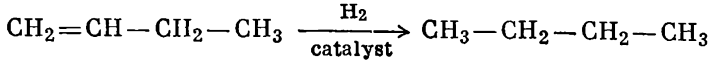


### Addition to Compounds with Conjugated Carbon-Carbon Double Bonds

The distinctive features of compounds with conjugated carbon-carbon double bonds are their high reactivity (in addition reactions) and their ability to add halogens, hydrogen halides, etc., in the 1,4-position.

The elevated addition reactivity of substances with conjugated double bonds can be illustrated, for example, by comparing the hydrogenations of butylene and butadiene.

Butylene generally* is not hydrogenated by nascent hydrogen; it adds hydrogen only in the presence of a catalyst.



* An exception is hydrogenation of monoalkenes by hydrogen released from calcium-ammonia $Ca(NH_3)_6$ [49].

Butadiene, however, can add nascent hydrogen to form butene-2.

$$CH_2=CH-CH=CH_2 \xrightarrow{2H} CH_3-CH=CH-CH_3$$

The latter is hydrogenated to butane only in the presence of a catalyst.

The tendency of compounds with conjugated double bonds to yield 1,4-addition compounds is illustrated by the following examples:

$$CH_2=CH-CH=CH_2+Br_2 \longrightarrow Br-CH_2-CH=CH-CH_2-Br$$

$$CH_3-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH=CH_2+Br_2 \longrightarrow Br-\underset{\displaystyle CH_3}{\underset{|}{CH}}-\underset{\displaystyle CH_3}{\underset{|}{C}}=CH-CH_2Br$$

$$CH_2=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH=CH_2+Br_2 \longrightarrow Br-CH_2-\underset{\displaystyle CH_3}{\underset{|}{C}}=CH-CH_2Br$$

In all these cases, however, 1,2-dibromides are also formed.

Depending on the nature of the reagent addition to a conjugated system may occur in the 1,4- or in the 1,2-positions; for example, in the case of muconic acid:

$$HOOC-CH_2-CH=CH-CH_2-COOH$$

$$\uparrow H_2$$

$$HOOC-CH=CH-CH=CH-COOH$$

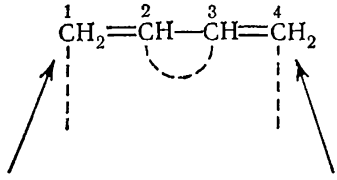
$$\downarrow Br_2$$

$$HOOC-\underset{\displaystyle Br}{\underset{|}{CH}}-\underset{\displaystyle Br}{\underset{|}{CH}}-CH=CH-COOH$$

To explain 1,4-addition in conjugated systems Thiele proposed a hypothesis of partial valences [50]. According to this hypothesis unsaturated carbon atoms linked by double bonds do not fully use up their chemical affinity, as a result of which each of these carbon atoms has a "residual affinity" or "partial valence", for example:

$$\overset{1}{C}H_2=\overset{2}{C}H-\overset{3}{C}H=\overset{4}{C}H_2$$

The partial valences of neighbouring atoms (2 and 3) are mutually saturated, so that the most unsaturated atoms are 1 and 4, where addition takes place:

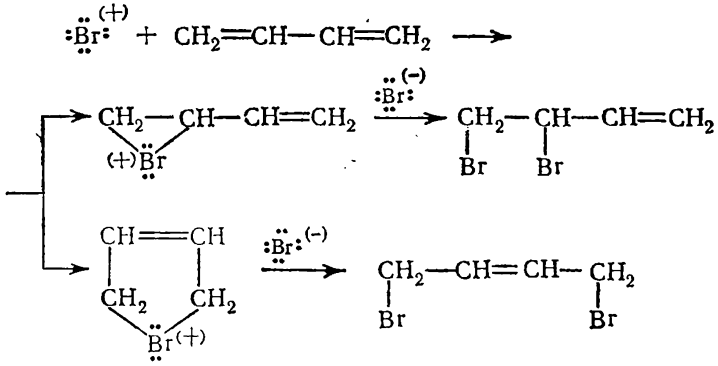


From the point of view of Thiele's hypothesis 1,4-additions seem natural and comprehensible, but it cannot be understood why 1,2-additions also take place (and sometimes predominantly) together with the 1,4-additions.

The inability to explain 1,2-additions is the weak point of Thiele's hypothesis.

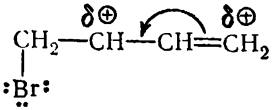
Recently a mechanism was proposed for addition reactions to conjugated double bonds, analogous to the mechanism of addition to compounds with isolated double bonds.

According to this mechanism, the addition, say, of a halogen to butadiene, begins with addition of the halogen cation, followed by the formation of a three- or a five-membered cyclic onium cation



Three-membered and five-membered onium cations react with bromine anions to form 1,2- and 1,4-additions, respectively.

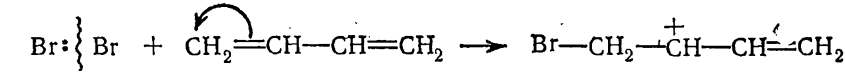
It should, however, be taken into consideration that the formation of the onium ring must be more difficult in this case than in that of addition to alkenes, because after $Br^+$ addition neither the second nor the fourth carbon atom has



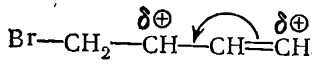
a whole positive charge as in the addition of a halogen cation to the alkene (page 217). In the case of 1,4-addition of hydrogen halides the formation of onium rings is entirely out of the question.

Because of this the following reaction mechanism is evidently more correct [51].

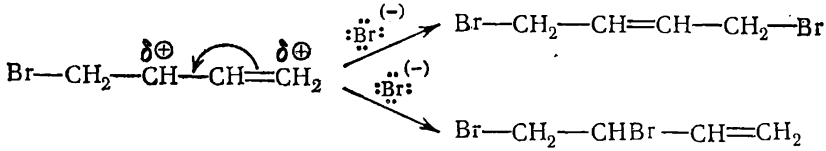
In the first step the halogen cation (or a proton) adds to butadiene*



In the cation formed the positive charge is not localized on the second carbon atom because of the fact that the π-electron pair of the neighbouring double bond shifts towards it:

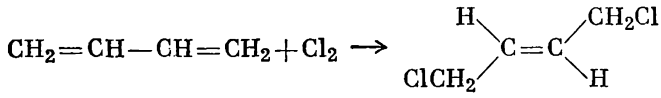


In the second step of the reaction the bromine anion may attack either the second or the fourth carbon atom:



The ratio of 1,4- and 1,2-dibromides formed depends on the reaction conditions as well as on the stability of the resulting compounds.

Investigation of the stereochemistry of 1,4-addition of chlorine to butadiene showed [58] this to be a reaction of *trans*-addition; the reaction product contains chloromethyl groups in *trans*-positions.



This result indicates that the addition of chlorine to butadiene is not a one-stage process; therefore the cyclic transition state (III)

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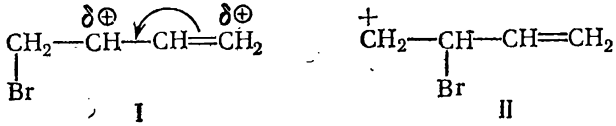
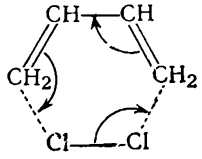
* That $Br^+$ adds to the first and not to the second carbon atom may be concluded from the following discussion. If $Br^+$ adds to the first carbon atom, cation I forms and if it adds to the second carbon atom, cation II results.



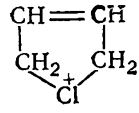
The energy of cation II is higher because its positive charge is localized on a single carbon atom, and therefore the reaction proceeds through cation I.

should be excluded from consideration.



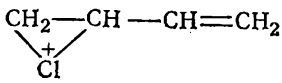
III

It is also evident that the *trans*-product cannot form from the five-membered chloronium cation IV:

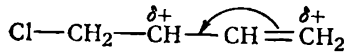


IV

The *trans*-product can form from the transition cations (V) or (VI)



V



VI

Usually the addition of chlorine to butadiene at a moderate temperature results in the 1,2-adduct. As the reaction temperature is increased the percentage of the 1,4-addition product increases, because the activation energy of the 1,4-addition is higher than that of the 1,2-addition.

On the other hand, the 1,4-dichloride is thermodynamically more stable than the 1,2-dichloride. This is evident, for example, from the fact that if the mixture of products obtained at room temperature is heated with $ZnCl_2$ to 200° and higher, an equilibrium mixture is formed containing about 70% 1,4-dichloride [54].

Thus the result of the reaction at low temperatures is determined by the kinetic factor: the less stable isomer forms faster.

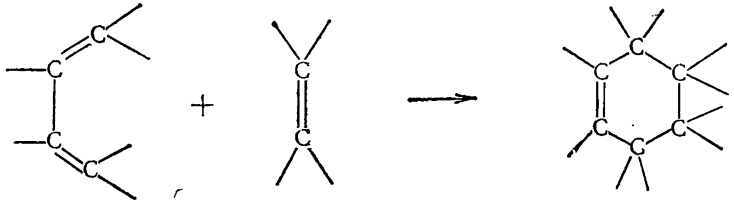
An analogous picture is observed in the addition reactions of bromine to cyclopentadiene, 1,3-cyclohexadiene and butadiene (in nonpolar solvents), as well as in reactions of hydrogen chloride and hydrogen bromide with butadiene. In all these cases the reaction mixtures contain the 1,2-adduct in greater quantities than is contained in the equilibrium mixtures of 1,2- and 1,4-adducts.

However, it is still impossible to give a satisfactory answer to the questions why the adducts of 1,4-additions are thermodynamically more stable and why the products of 1,2-addition form faster in the course of the reaction [55]. Further kinetic and stereochemical investigations are needed.

**Diene Synthesis (Diels-Alder Reaction) [56]**

Addition to dienes of substances of the unsaturated series (dienophiles), the molecules of which often (but not always) contain electron-attracting groups conjugated with the C = C bond, is called *reaction of diene synthesis* or *Diels-Alder reaction.*

This reaction results in the formation of six-membered rings

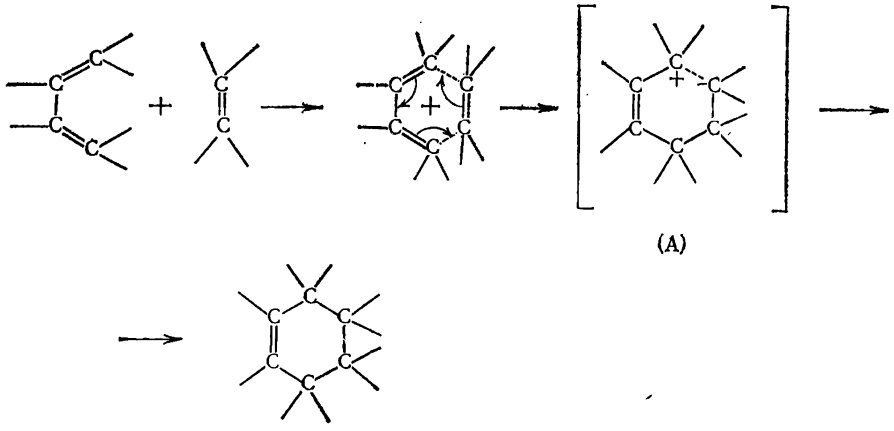


Diene Dienophile Adduct

In the course of the Diels-Alder reaction a redistribution of electron density takes place, as a result of which two new single bonds are formed, three double bonds are converted into single ones and one single bond becomes a double bond.

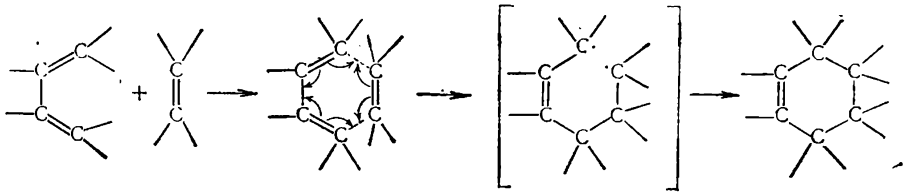
It is quite impossible so far to decide whether the nature of the diene synthesis is heterolytic or homolytic. The difference between these mechanisms is illustrated in the two following schemes:

Heterolytic mechanism



(A)

Homolytic mechanism



(B)

(in the latter case the bent arrows indicate shift of a single electron).

It is quite probable, that depending on the structure of the reacting substances and on the reaction conditions diene synthesis may follow a heterolytic mechanism in some cases and a homolytic in others.

The kinetics of the reaction (first-order with respect to diene, and first-order with respect to dienophile) [57] gives no clue as to which of these two mechanisms is valid.

The fact that the reaction of diene synthesis is not accelerated by peroxides does not preclude the homolytic mechanism, inasmuch as peroxides are effective only in the production of monoradicals; and monoradicals are much more apt to take part in various side reactions than to be converted into biradicals.

It is interesting that diene synthesis reactions are more sensitive to the polarity of the solvent than typical free-radical reactions, but less sensitive than ordinary heterolytic reactions [58].

Whether the mechanism of diene synthesis is heterolytic or homolytic, the transition bipolar ion (A) or biradical (B) exists a very short time because the Diels-Alder reaction proceeds as a *cis*-addition.

Otherwise a mixture of *cis*- and *trans*-addition products would result. Many investigators think that both single bonds are formed simultaneously and that the bipolar ion (A) and the biradical (B) do not exist at all [59].

On the other hand, in a number of cases certain peculiarities of the dependence of diene and dienophile reactivity in the Diels-Alder reaction on their structure favour the two-stage mechanism of diene synthesis.

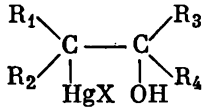
For example, electron-donor groups (of the alkyl or alkoxyl type) in the diene molecule and electron-acceptor groups (of the carboxyl or cyano group types) in the dienophile molecule accelerate the reaction. These data are in agreement with the concept of the formation of a bipolar ion (A); however, they may also be interpreted in favour of the preliminary formation of an unstable complex of the diene with the dienophile, with a subsequent redistribution of bonds [60].

Diene synthesis reactions are catalyzed in some cases by acids. This can be explained by coordinational addition of a proton to the dienophile molecule, which becomes more polarized and more reactive owing to the electrons being pulled away from the reactive centre.

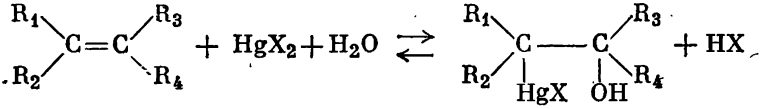
### Addition of Heavy Metal Salts to Ethylenic Compounds

Of the reactions of heavy metal salts with unsaturated hydrocarbons the most investigated ones are the addition reactions of mercury salts to ethylenic and acetylenic compounds [133].

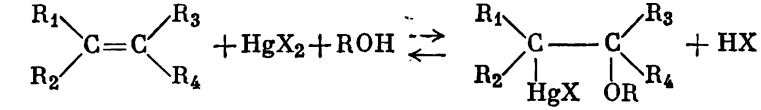
In aqueous solution the addition of well-dissociating mercury salts (nitrate, sulphate, acetate) to ethylenic compounds takes place. The substances formed

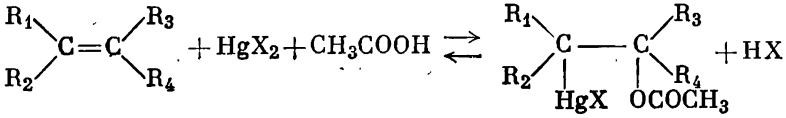


are products of the addition to the double bond of the HgX and OH radicals.



The reaction takes a similar course in alcohol or in acetic acid:





The addition of mercuric salts to alkenes follows Markovnikov's rule, i.e., the mercury atom joins the less hydrogenated carbon atom.

**Effect of the Alkene Structure.** The structure of the alkene has a noticeable effect on the rate of reaction.

*Trans*-alkenes in general react more sluggishly than their *cis*-isomers. Thus, fumaric, mesaconic and cinnamic acids do not give addition products in aqueous media, while maleic, citraconic and allocinnamic acids add mercury salts normally. The presence of electron-acceptor groups next to the double bond impedes the reaction.

It is interesting to note that highly branched alkenes react sluggishly with mercuric salts even when the unsaturated carbon atoms have electron-donor groups attached to them. Thus, tetramethylethylene does not react with mercury salts, while unsymmetrical diphenylethylene reacts slowly, yielding a normal addition product.*

It should be noted that no 1,4-additions of mercuric salts to conjugated dienes or to the α-, β-unsaturated ketones have ever been observed: addition always takes place in the 1,2-position.

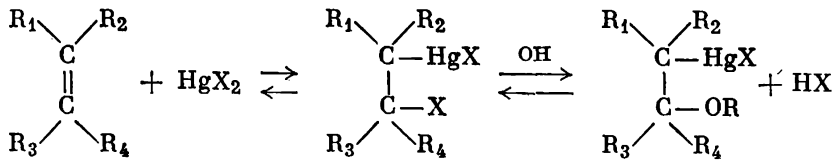
**Effect of Reaction Conditions.** The pH of the medium is of great importance in the addition of mercuric salts to alkenes. In spite of the fact that acids impede the addition of mercuric salts, the latter do not add in an alkaline solution. The reaction proceeds best if the aqueous solution of the mercuric salt is carefully neutralized until a basic salt is formed. The latter dissolves when a small amount of alkene is added, after which the reaction mixture is treated carefully with more caustic solution, etc.

The direction and rate of the reaction are influenced perceptibly by the nature of the mercuric salt used. It is best to use nitrates and acetates, because they add rapidly without yielding significant quantities of by-products. Neutralization of the acid formed during the reaction is more important in mercuric nitrate than in mercuric acetate addition, because acetic acid is not a sufficienty strong acid to reverse the reaction to a significant degree.

Addition of mercuric salts takes place more smoothly at room temperature. Higher temperatures cause reduction of the mercuric salts and the formation of undesirable reaction by-products.

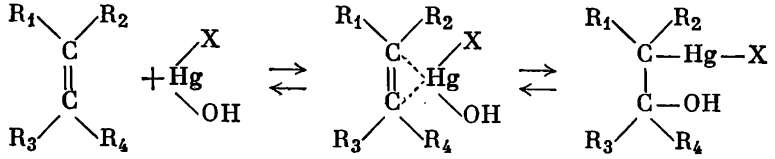
A number of catalysts are known, which accelerate the addition of mercuric salts to alkenes in nonaqueous solvents. For example, the addition of $HgX_2$ to alkenes in methanol is accelerated considerably by peroxides, nitric acid and boron trifluoride etherate.

**Mechanism of Addition of Mercuric Salts to Alkenes.** Until 1935 most investigators held that initially the alkene adds a molecule of mercuric salt, after which the compound formed reacts with the solvent yielding the end product of the reaction:



* Steric hindrance evidently plays a more important part in addition reactions of mercuric salts to alkenes than in hydrogen halide addition. This is due to the fact that the mercury cation is much larger than the proton.

Sand expressed a different viewpoint having an external resemblance with the currently prevalent point of view. He considered that a coordination complex compound of the alkene with the base salt is formed first through the partial valences of the alkene, and then this complex compound rearranges into the final product:



These points of view are now of historical interest only.

The results of a study of the equilibrium between cyclohexene and aqueous mercuric nitrate were the only material proof of the existence of a coordination complex of alkenes with mercuric salts.

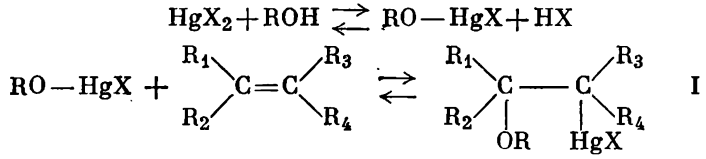
These results can be reasonably explained only by assuming the existence of two rapidly established equilibria [61]:

$$C_6H_{10}+Hg^{++} \rightleftarrows C_6H_{10}\cdot Hg^{++}$$

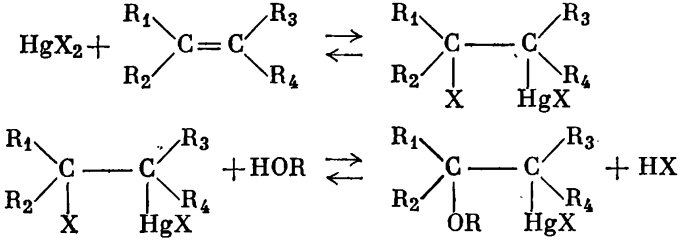
$$C_6H_{10}+Hg^{++}+H_2O \rightleftarrows C_6H_{10}\cdot{}^{+}HgOH+H^{+}$$

The latter equilibrium is the more important.

Addition of mercuric salts to alkenes proceeds as a second-order reaction which confirms scheme I

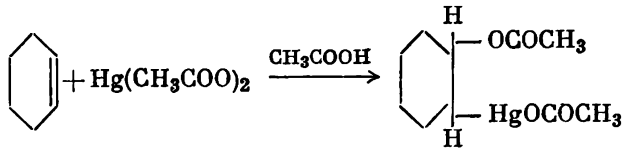


according to which alcoholysis (hydrolysis) of the mercuric salts precedes addition. If the reaction followed scheme II

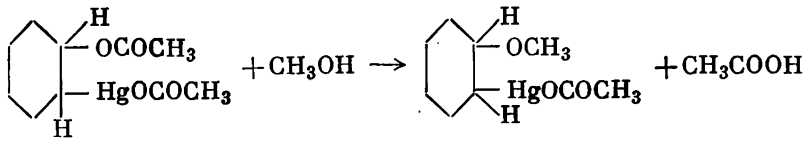


the order of the reaction would be determined by the alcoholysis (special investigations have established that addition is faster). But alcoholysis must proceed as a pseudomonomolecular reaction because of the large excess of alcohol.

In order to confirm mechanism I the adduct of cyclohexene to mercuric acetate (in acetic acid) was prepared:

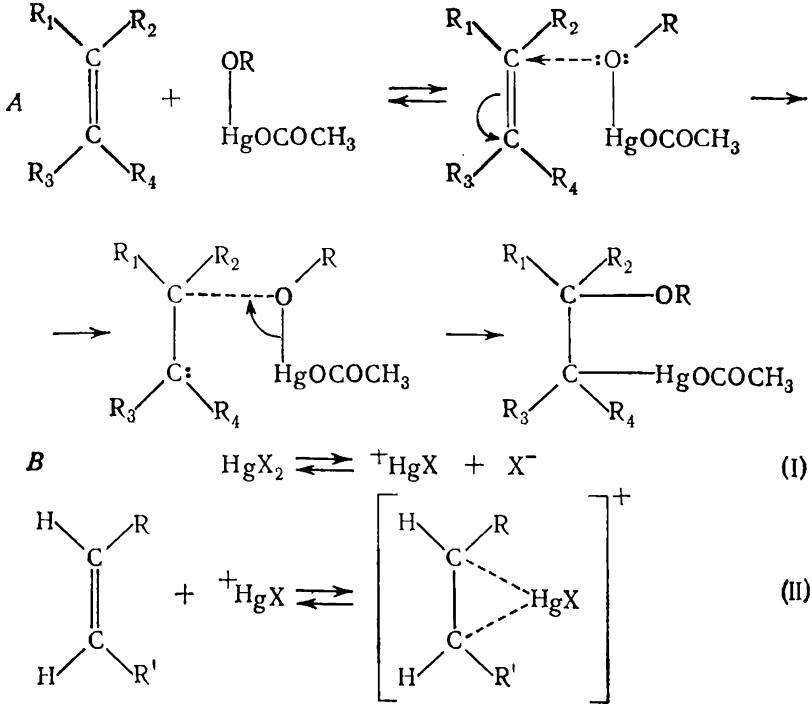


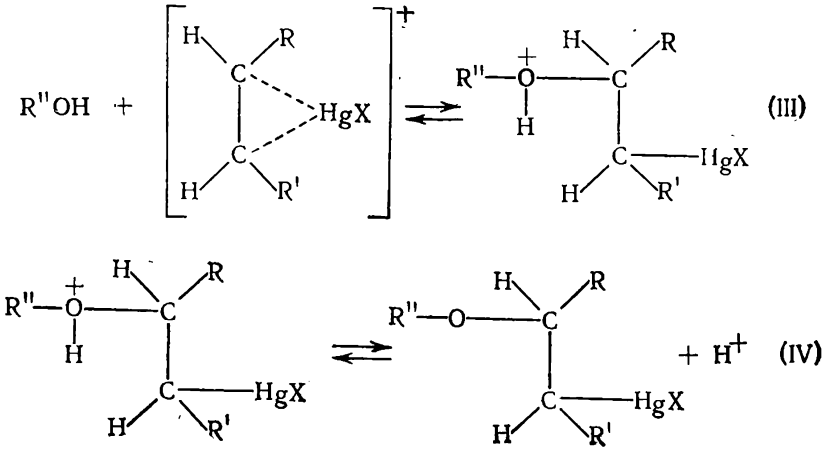

The latter was subjected to alcoholysis in methanol:




A study of the kinetics of these reactions (addition of mercuric acetate and alcoholysis with methanol) showed that both proceed so slowly that the addition of mercuric salts to alkenes according to mechanism II becomes improbable because of kinetic considerations.

At present the two mechanisms of the addition of mercuric salts to alkenes given below are considered more likely:





Mechanism *A* consists of molecular addition of an alkoxy (or basic) mercuric salt to the alkene. Although the presence of methoxymercuric acetate in the methanolic solution of mercuric acetate has not been proved, it is assumed that it may exist in an equilibrium system, and that its formation is rapid.

Mechanism *B* is an ionic one.

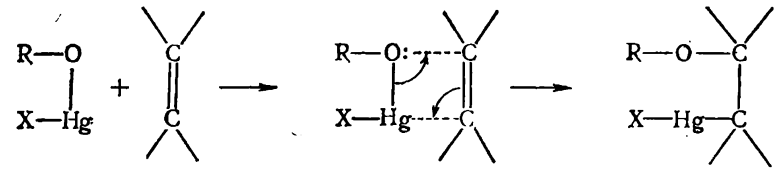
The configuration of the alkene is retained throughout the reaction owing to the free electron pair of the carbanion in the first case, and to the formation of a cyclic cation, in the second.

*Trans*-addition should occur when the reaction proceeds according to mechanism *B*, and *cis*-addition or mixed *cis*- and *trans*-additions, if it follows mechanism *A*.

Until recently the ionic mechanism was preferred, because (by analogy with additions of halogens and hydrogen halides) it was thought that the addition of mercuric salts to alkenes is always a *trans*-addition.

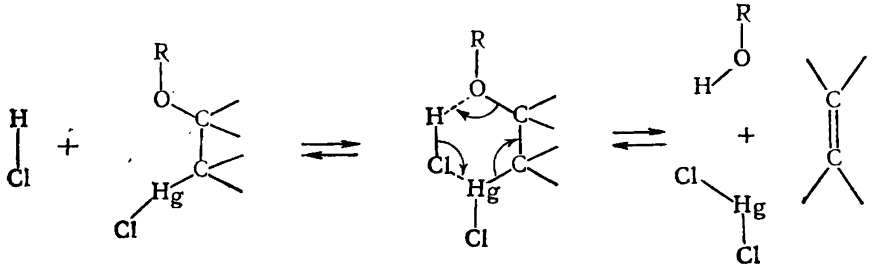
However Wright [62] established that hydroxymercuration of Δ′-terpineol is actually a *cis*-addition. He also obtained kinetic data which testified against the participation of ions in the addition of mercuric salts to alkenes [63].

According to Wright [63] the reaction mechanism consists in four-centre *cis*-addition of the basic mercuric salt to the alkene:



This scheme is in agreement with kinetic (first-order with respect to each of the reacting components) and stereochemical (*cis*-addition) data. The substances react as molecules or ionic pairs but not as free ions.

The mechanism under consideration is analogous with the reaction mechanism of deoxymercuration (decomposition of adducts by acids into an alkene and a mercuric salt)



Here, a hydrogen chloride molecule participates in the cyclic transition state besides the alkene and the basic salt [64].

It must, however, be taken into consideration that different stereochemical paths of the hydroxymercuration reaction are possible, depending on the structure of the alkene and the reaction conditions.

Thus, a study of the NMR spectra of the products of hydroxymercuration of cyclohexene (I) and 2-norborene (II) supported *trans*-addition in case I and *cis*-addition in case II [65]. In the case of cyclohexene *trans*-addition was proved recently by calculation [66] of the optical rotation of the methoxymercuration product according to Brewster's rule [67].

Arsenous chloride adds to alkenes in the same way as mercuric salts, e.g.:

$$CH_2{=}CH_2 + AsCl_3 \longrightarrow Cl{-}CH_2{-}CH_2{-}AsCl_2$$

The reaction takes place without a solvent in the presence of aluminum chloride. The stereochemistry and kinetics of this reaction have not been studied.

In distinction from the above-mentioned mercuric and arsenous compounds numerous addition products of alkenes to salts of silver, copper, zinc, palladium, platinum, such as $(CH_3)_2C = CH_2 \cdot 2ZnCl_2$; $KCl \cdot PtCl_2 \cdot C_2H_4$; $PtCl_2 \cdot C_2H_4$, are complexes rather than organometallic compounds.

### Addition of Heavy Metal Salts to Acetylenic Hydrocarbons

The first investigations of the addition of mercuric salts to acetylene hydrocarbons were carried out by Kucherov [68], who established the composition of the compounds obtained by him from

acetylene and allylene, and obtained acetaldehyde and acetone by acid decomposition of the adducts. This reaction is of great industrial importance.

At present acetaldehyde is synthesized commercially by adding water to acetylene in the presence of mercuric sulphate and sulphuric acid.

$$H-C\equiv C-H+H_2O \xrightarrow[(H_2SO_4)]{Hg^{++}} CH_3-C\overset{O}{\underset{H}{<}}$$

The reaction passes through the stage of an addition product of the mercuric salt to acetylene. This product decomposes in sulphuric acid, yielding acetaldehyde.

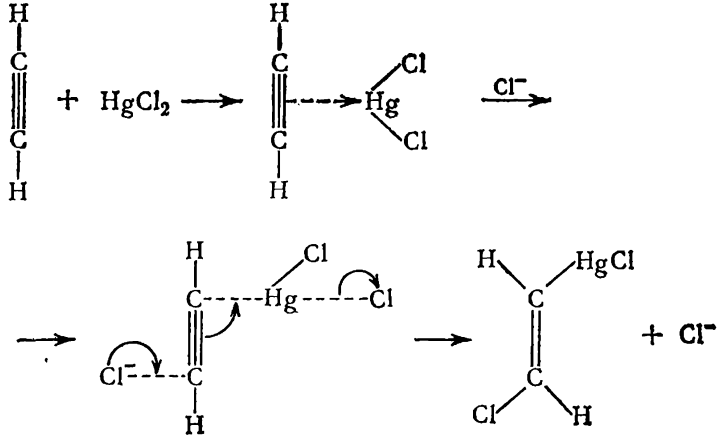
Addition of mercuric salts to unsymmetrical acetylene hydrocarbons follows Markovnikov's rule, for instance:

$$CH_3-C\equiv CH+HgCl_2 \longrightarrow CH_3-CCl=CHHgCl$$

The reaction of acetylene with mercuric chloride in aqueous solution was investigated the most thoroughly. This reaction proceeds according to the equation:

$$H-C\equiv C-H+HgCl_2 \longrightarrow \begin{matrix} Cl & & H \\ & C=C & \\ H & & HgCl \end{matrix}$$

The optimum yield of reaction products is obtained by saturating with acetylene a strong solution of mercuric chloride in 15% hydrochloric acid [69]. The reaction proceeds exclusively in the *trans*-position. The kinetics of the reaction was studied by Smirnov-Zamkov and Shilov [70] who showed that, as in the case of hydrogen halide addition, a π-complex of acetylene and mercuric chloride, $C_2H_2 \cdot HgCl_2$, is formed first, and this reacts with the chloride anion in the second stage of the reaction.



Acetylenic compounds add arsenic trihalides or alkyl (aryl) dichloroarsines in the presence of $AlCl_3$ to form a mixture of arseno-organic compounds according to the scheme below:

$$nRC \equiv CR' + AsCl_3 \longrightarrow (RCCl{=}CR')_nAsCl_{3-n}$$
$$nRC \equiv CR' + R''AsCl_2 \longrightarrow (RCCl{=}CR')_nAs(Cl_{2-n})R'',$$

where R and R′ = alkyl, aryl, hydrogen, carboxyl; R″ = alkyl, aryl, chlorine; $n = 1, 2, 3$.

Under similar conditions acetylene adds antimony pentachloride (in the presence of mercuric chloride).

$$HC \equiv CH + SbCl_5 \xrightarrow{(HgCl_2)} ClCH{=}CHSbCl_4$$

### 4-1.2 Nucleophilic Addition to Unsaturated Compounds

The above-mentioned reactions of addition of halogens and hydrogen halides and heavy metal salts to unsaturated compounds begin by a cation attacking the unsaturated molecule and are therefore reactions of electrophilic addition.

The presence of electron-donor groups in the vicinity of the double bond favours electrophilic addition reactions, while electron-acceptor groups impede these reactions (page 223). The presence of strong electron-acceptor groups in the vicinity of the double bond may be expected to decrease the electron density of the double carbon-carbon bond, and consequently, to impede the electrophilic addition to such an extent that this may lead to the simultaneous or even predominant occurrence of nucleophilic addition reactions starting with an anion attacking the unsaturated molecule.

This assumption has been confirmed experimentally.

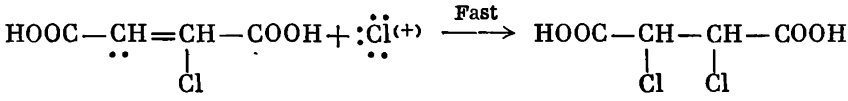
Thus, it was found that the addition of halogens to maleic and fumaric acids, vinyl bromide and allyl chloride is accelerated by lithium chloride or bromide [71], i.e., is catalyzed by halide anions. Since of the two steps of the addition of a halogen to an alkene, only the first—addition of the halide cation or anion to the alkene—is a slow process, the first step in the cases cited above is apparently the addition of the anion to the alkene, e.g.:

$$HOOC{-}CH{=}CH{-}COOH + Cl^- \xrightarrow{\text{Slow}} HOOC{-}\underset{\cdot\cdot}{CH}{-}\underset{|}{CH}{-}COOH$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad Cl$$

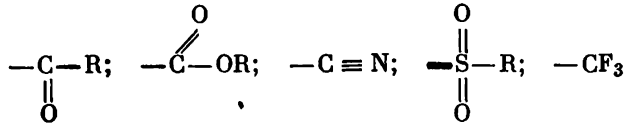
Adding LiCl accelerates this reaction because of the increase in chloride anion concentration.

The second step of the reaction, which is a purely ionic process, proceeds faster and for that reason cannot influence the rate of

addition of the halogen to the unsaturated compound.



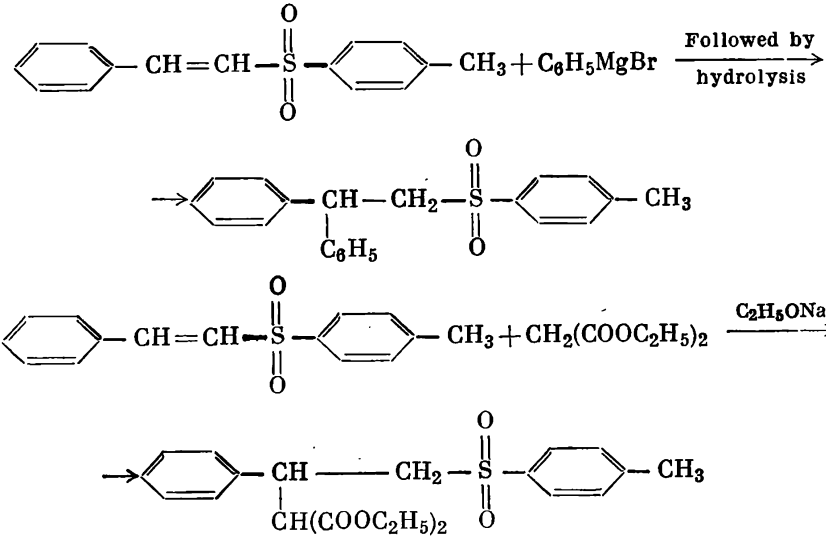
The nucleophilic type of addition reactions is comparatively rare. It is limited mostly to compounds in which the double bond is under the influence of such strongly electron-acceptor groups as



and which are subject to the action of such strong nucleophilic reagents as RMgX; NaOAlk; KCN.

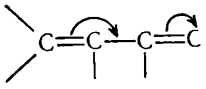
We may mention a few more examples of nucleophilic addition.

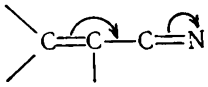
Nucleophilic additions include additions of phenylmagnesium bromide, alcohol or a malonic ester to vinyl sulphones. These reagents ordinarily do not add to isolated double bonds.



Ability to add nucleophilic reagents is exhibited by α,β-unsaturated ketones, aldehydes, nitriles. The carbon-carbon double bond in these compounds is much less active with regard to electrophilic reagents, while the carbonyl group shows decreased activity towards nucleophilic reagents. The cause of this phenomenon is conjugation of the carbon-carbon multiple bonds with carbon-oxygen (or carbon-

nitrogen) bonds:





The reaction of ethyl cinnamate with malonic ester in the presence of a basic catalyst may serve as an example of a nucleophilic addition:

$$C_6H_5-CH=CH-COOC_2H_5 + CH_2(COOC_2H_5)_2 \xrightarrow{C_2H_5ONa} C_6H_5-\underset{\displaystyle CH(COOC_2H_5)_2}{\underset{|}{CH}}-CH_2-COOC_2H_5$$

In many cases of nucleophilic addition to $\alpha,\beta$-unsaturated compounds it is not clear whether the addition takes place at the carbon-carbon double bond or whether 1,4-addition takes place first, followed by a rearrangement leading to ketonization.

Thus, the addition of a Grignard reagent to benzalacetophenone may take place by two different mechanisms:

I

$$C_6H_5-\overset{\delta\oplus}{CH}=\overset{\delta\ominus}{CH}-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5 + R-MgX \longrightarrow$$

$$\longrightarrow C_6H_5-\underset{\displaystyle R}{\underset{|}{CH}}-\underset{\displaystyle MgX}{\underset{|}{CH}}-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5 \xrightarrow{H_2O}$$

$$\longrightarrow C_6H_5-\underset{\displaystyle R}{\underset{|}{CH}}-CH_2-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5$$

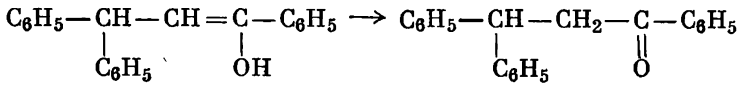
II

$$C_6H_5-\overset{\delta\oplus}{CH}=CH-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5 + R-MgX \longrightarrow$$

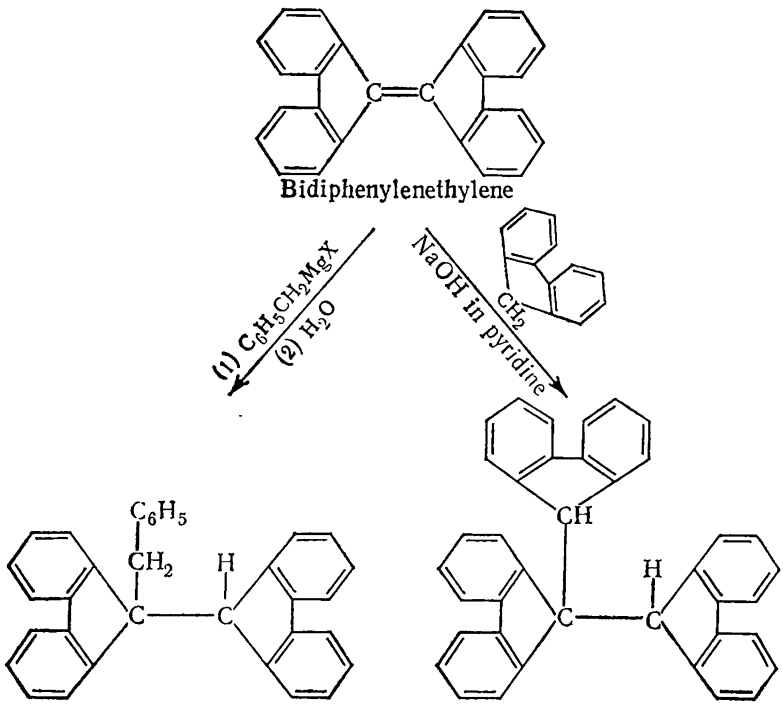
$$\longrightarrow C_6H_5-\underset{\displaystyle R}{\underset{|}{CH}}-CH=\underset{\displaystyle OMgX}{\underset{|}{C}}-C_6H_5 \xrightarrow{H_2O}$$

$$\longrightarrow \left[C_6H_5-\underset{\displaystyle R}{\underset{|}{CH}}-CH=\underset{\displaystyle OH}{\underset{|}{C}}-C_6H_5\right] \longrightarrow C_6H_5-\underset{\displaystyle R}{\underset{|}{CH}}-CH_2-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5$$

That 1,4-addition (mechanism II) actually takes place in this reaction was proved by isolating the pure crystalline enol resulting from the hydrolysis of the magnesium enolate. This enol changed slowly into its isomeric ketone



However, reactions of nucleophilic addition to α,β-unsaturated compounds are known where 1,4-addition is impossible, for example [72]:




1,4-addition is also impossible in the case of perfluoroalkenes (page 266).

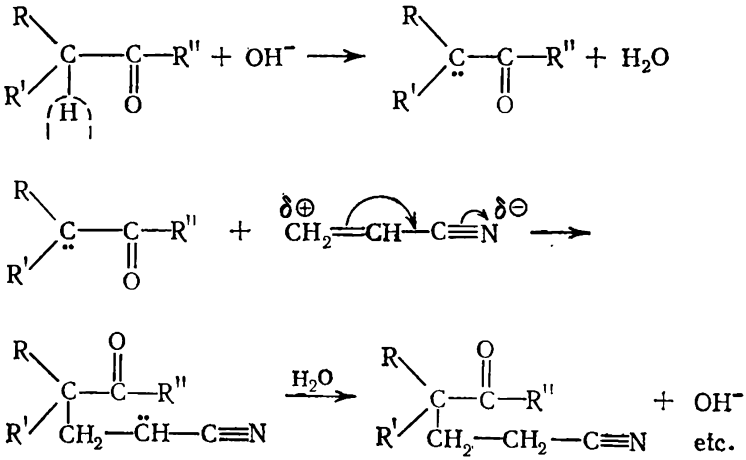
Owing to the strong electron-acceptor effect of the nitrile group

the double bond in acrylonitrile exhibits high reactivity toward nucleophilic reagents.

Acrylonitrile adds not only to amines, alcohols, phenols and hydrogen sulphide, but also to compounds having a reactive meth-

ylene or methine group (ketones, aldehydes, nitro compounds). Such an addition is called a *cyanoethylation reaction*, because the β-cyanoethyl group is substituted for the active hydrogen atom.

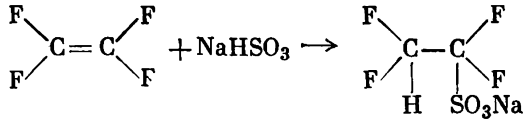
The mechanism of this reaction may be formulated, in the case of cyanoethylation of ketones, for example, as follows:



Fluorine atoms possess strong electron-acceptor properties; therefore their accumulation at the carbon-carbon double bond decreases its electron density so much that perfluoralkenes are true electrophilic compounds, in contrast to alkenes. For example, tetrafluoroethylene adds electrophilic agents such as hydrogen bromide with difficulty.

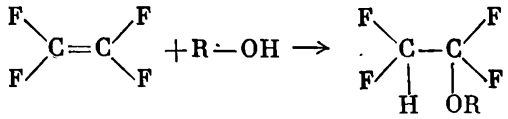
On the other hand, addition of nucleophilic reagents proceeds easily [73], these reactions being accelerated by basic catalysts.

In aqueous solutions of bisulphite the addition of $HSO_3^-$ proceeds with the formation of sodium tetrafluoroethane sulphonate:

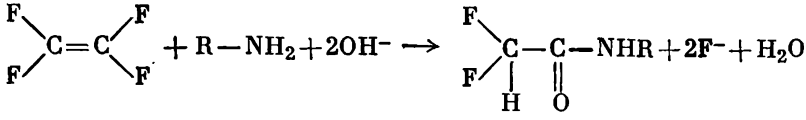


(simultaneously hydrolysis takes place, resulting in difluoroacetic acid).

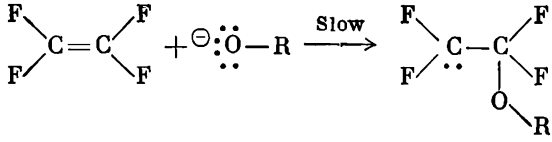
In the presence of alcoholates tetrafluoroethylene easily adds alcohols:



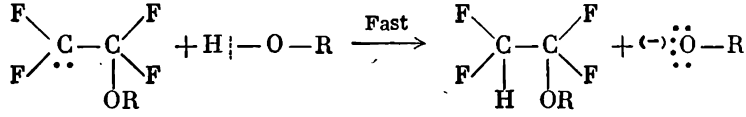
Tetrafluoroethylene reacts with aliphatic amines under the same conditions:



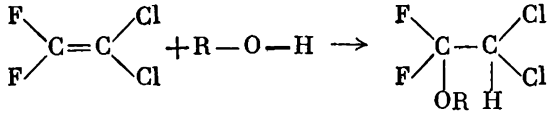
All these reactions of perfluoroalkenes resemble reactions of addition to aldehydes and ketones. The first step, undoubtedly, is the attack of the anionoid part of the reagent molecule on the alkene, e.g.:



In the second step the carbanion formed adds quickly the cationoid part of the reagent molecule



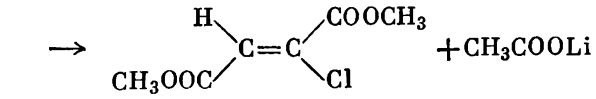
In addition reactions to fluoroalkenes of unsymmetrical structure the anion of the adding molecule forms a bond with the most fluorinated carbon atom, for example:



This is due to the C—F bond being more polarized than the C—Cl bond, and therefore the carbon atom linked to the fluorine carries a greater positive charge, facilitating the attack of the anion.

E. A. Shilov and A. E. Shilov [74] observed nucleophilic additions of hydrogen halides to certain acetylenic derivatives.

A study of the addition of hydrogen halide to dimethyl acetylenedicarboxylate revealed that solutions of lithium chloride in glacial acetic acid are capable of adding HCl to the acetylenedicarboxylic acid ester



The resulting chlorofumaric ester is incapable of adding HCl under the same conditions.

It is interesting that at the same concentration of reagents and other equal conditions the addition of HCl from a solution of LiCl in acetic acid is faster than in HCl proper.

The addition of HCl from a solution of LiCl in $CH_3COOH$ obeys the equation

$$-\frac{dc}{dt} K_2 AC$$

where $A$ = the concentration of the acetylenedicarboxylic ester, $C$ = the concentration of chloride and $K_2 = 3.4 \times 10^{-4}$ mole·l$^{-1}$··min$^{-1}$ at 30°. With free hydrogen chloride the addition also proceeds as a second-order reaction but $K_2 = 0.9 \times 10^{-4}$ mole·l$^{-1}$·min$^{-1}$ at 30°.

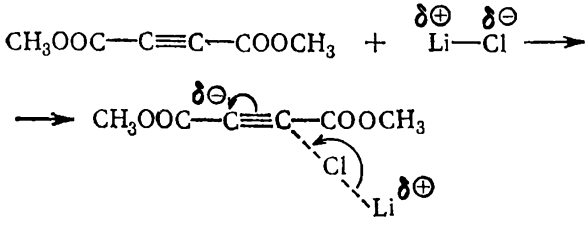
When the solution contains LiCl and HCl together, they react with the acetylenedicarboxylic ester independently of each other. Other strong acids, such as trichloroacetic acid, have no influence on the rate of the reaction with LiCl.

Undissociated molecules of acetylenedicarboxylic acid react almost equally fast with aqueous solutions of NaCl and HCl. Evidently, the rate of addition of HCl depends on the concentration of chloride-ion and is independent of the hydrogen-ion concentration.

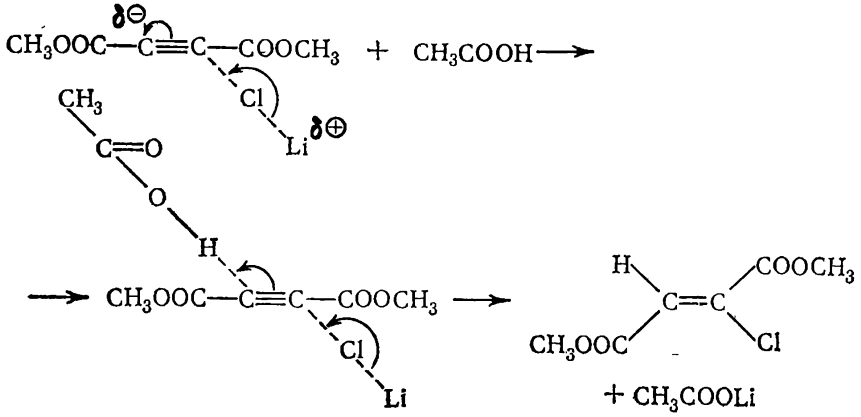
Neither the neutral nor the acid salt of acetylenedicarboxylic acid react noticeably with chloride salts in aqueous or acetic acid solution.

Bromine and iodine salts behave much like lithium chloride but are much more active. LiBr in glacial acetic acid reacts with the acetylenedicarboxylic ester approximately five times faster than LiCl; HI adds from a KI solution (in 80% glacial acetic acid) 260 times faster than HCl from LiCl under similar experimental conditions.

The above experimental data point to the conclusion that the addition reaction of HCl from salt solution to the acetylenedicarboxylic ester starts with a nucleophilic attack by the LiCl molecule on the acetylene compound:



In the second step of the reaction a molecule of acetic acid reacts with the LiCl complex of acetylenedicarboxylic ester:



The rate of reaction is limited, however, by the reaction of the acetylenic compound with LiCl and the second step is not reflected in the kinetic equation.

If this reaction mechanism is accepted, the lower activity of HCl molecules as compared with LiCl molecules can be understood because the nucleophilic affinity of HCl is lessened by the bond of chlorine with proton. The greater activity of LiBr, and particularly of LiI, compared to LiCl is also understandable because the nucleophilic strength of halide ions increases in the order: $F < Cl < < Br < I$.

The nucleophilic nature of the addition of HCl from solutions of chloride salts was confirmed in a study of the kinetics of certain analogous reactions.

It was established, for example, that exchange of the $-COOCH_3$ group for H or $C_6H_5$ slows down hydrogen halide additions.

The rate of addition of HI from a KI solution in 80% aqueous acetic acid decreases in the sequence:

$$CH_3OOC-C\equiv C-COOCH_3 > H-C\equiv C-COOCH_3 > C_6H_5-C\equiv C-COOCH$$

The reaction with methyl propiolate proceeds 70 times slower than with the acetylenedicarboxylic ester, while methyl phenylpropiolate practically does not react with KI under the same conditions. Hence, contrary to the reactions of electrophilic addition, elimination of the electron-acceptor group in this case causes deceleration of the reactions.

The lower reactivity of the salts of acetylenedicarboxylic acid as compared with the acid itself is due to the presence of negative

charges at the salt anions which impede the attack of the nucleophilic reagent or make it impossible.

$$CH_3OOC-C\equiv C-COO^- \quad \text{or} \quad {}^-OOC-C\equiv C-COO^-$$

## 4-1.3 Radical Addition to Unsaturated Compounds

### Radical Addition of Halogens

Above we have considered the heterolytic addition of halogens to alkenes in the liquid or gas phase. In the latter case the addition is a surface reaction, the rate of which depends on the nature of the walls of the reaction vessel. The reaction can be accelerated by photochemical activation. However, in this case, its mechanism changes from heterolytic to chain homolytic:

$$Cl\cdot + CH_2{=}CH_2 \longrightarrow Cl-CH_2-CH_2\cdot$$

$$Cl-CH_2-CH_2\cdot + Cl{:}Cl \longrightarrow Cl-CH_2-CH_2-Cl + \cdot Cl \quad \text{etc.}$$

Reactions of photochemical addition of chlorine or bromine to isomeric dichloroethylenes and tetrachloroethylene are also chain homolytic processes in the vapour phase, as well as in carbon tetrachloride solution.

Reactions of this type include the photochemical addition of chlorine to benzene to form hexachlorocyclohexane.

It is characteristic of the kinetics of all these reactions that the resultant rate in the liquid phase is proportional to the square root of the intensity of the absorbed light. It follows that each quantum of absorbed light goes to form two active particles giving rise to two chains

$$:\ddot{Cl}:\ddot{Cl}: \xrightarrow{h\nu} 2\cdot\ddot{Cl}:$$

Oxygen is a strong inhibitor of the homolytic addition of halogens to alkenes. If the reaction is carried out in the presence of a considerable amount of oxygen, alkene oxidation products can be separated from the reaction mixture. Thus, dichloroacetyl chloride, $CHCl_2-COCl$, was found to form during the photochemical addition of chlorine to trichloroethylene; trichloroacetyl chloride, $CCl_3-COCl$, was among the products of the reaction of addition of chlorine to tetrachloroethylene.

Since oxygen itself is incapable of reacting with alkenes under the conditions of these experiments, it has been assumed that oxygen reacts with some intermediate compound formed as a result of the attack of a halogen atom on the alkene. Had two halogen atoms

reacted with the alkene, the final dihalide would not have reacted with the oxygen.

Investigation of the photochemical addition of halogens to alkenes has shown that when small amounts of bromine in benzene solution are added in scattered light to styrene, stilbene, allyl chloride, allyl bromide and cinnamic acid, the reaction mixture absorbs oxygen only when bromine adds to the double bond [75].

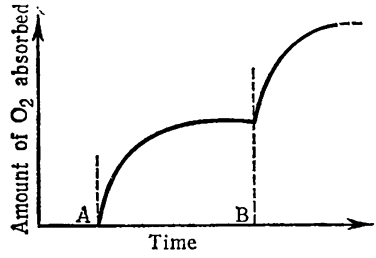



FIGURE 4-2 Addition of oxygen to an irradiated solution of alkene in carbon tetrachloride after addition of small amounts of bromine

Figure 4-2 illustrates the process of addition of oxygen to an irradiated solution of alkene in carbon tetrachloride directly after additions of small amounts of bromine (bromine is added at *A* and *B*).

The absorbed oxygen may be titrated quantitatively in the reaction product as peroxide. This is an indication that unstable peroxides form in the reaction products.

The mechanism of halogen addition to alkenes in the presence of oxygen is as follows. The atomic halogen formed during the photolysis of the molecular halogen (step *a*) adds to the alkene forming a free radical with an odd electron on the carbon (step *b*). The reaction of this radical with a halogen molecule results in the dihalide and atomic halogen (step *c'*).

In the presence of oxygen another process may take place simultaneously—addition of oxygen to the organic radical with the formation of an unstable peroxide radical (step *c''*)

(a) $Br : Br \xrightarrow{h\nu} 2 \cdot Br$

(b) $Br^{\bullet} + CH_2=CH-R \longrightarrow Br-CH_2-\overset{\bullet}{C}H-R$

(c) $Br-CH_2-\overset{\bullet}{C}H-R + Br : Br \longrightarrow Br-\overset{\bullet}{C}H_2-CHBr-R + \cdot Br$ etc.

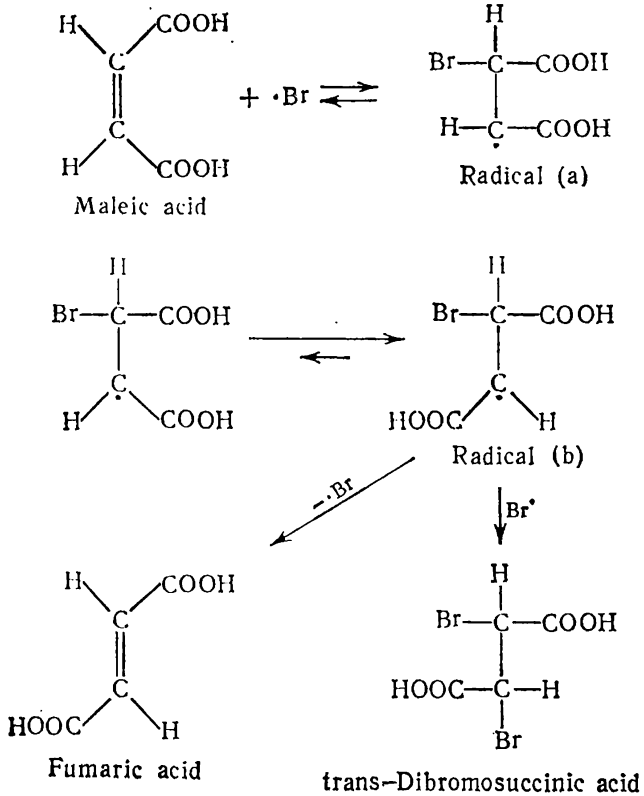
(c') $Br-CH_2-\overset{\bullet}{C}H-R + O_2 \longrightarrow Br-CH_2-\underset{\displaystyle O-O^{\bullet}}{\underset{|}{C}H}-R$

(c'') $Br-CH_2-\underset{\displaystyle O-O^{\bullet}}{\underset{|}{C}H}-R + \cdot Br \longrightarrow Br-CH_2-\underset{\displaystyle Br}{\underset{|}{C}H}-R + O_2$

This retards the chain reaction both owing to exchange of the active radical with an odd electron on the carbon for a much less active one, and to termination of the chain (step *c''*). On the other hand, the peroxide radical may initiate autoxidation.

### Stereochemistry of the Radical (Homolytic) Addition of Halogens

In the homolytic addition of halogens to alkenes *cis-trans*-isomerization is observed. For example, *cis-trans*-isomerization of maleic acid to fumaric acid takes place readily in solution when small amounts of bromine or iodine are added and when the solution is irradiated with ultraviolet light. Under slight exposure the rate of isomerization is proportional to the square root of the light intensity and to the halogen concentration; however, if more light energy is available than the solution can absorb, the rate becomes proportional to the square root of the halogen concentration. It follows that the rate-determining step of this isomerization is the photolysis



of the halogen molecules into two atoms. Each atom formed then adds to the double bond to form the intermediate radical (*a*), which is capable of free rotation. If the radical formed loses its bromine atom in state (*a*), the initial maleic acid is regenerated. However, owing to the electrostatic repulsion of carboxyl groups, the intermediate radicals may be in state (*b*) wherein the carboxyl groups are at a maximum distance from each other (*trans*-position). When radical (*b*) loses a bromine atom, the *trans*-isomer, fumaric acid, results.

When a second bromine atom adds to radical (*b*) we get *trans*-dibromosuccinic acid.

The above mechanism for the homolytic addition of halogens to unsaturated compounds clears up not only the cause of *cis-trans*-isomerization, but predominant *trans*-addition in such compounds as maleic and allocinnamic acids, as well. The intermediate radicals may dimerize, losing bromine. It is known that this is just how truxillic and truxinic acids are formed.

Alkali metals, nitric oxide and benzoyl peroxide are also catalysts in the *cis-trans*-isomerization of alkenes. All these substances are radical reagents having an odd electron.

Benzoyl peroxide causes rapid isomerization of isostilbene to stilbene in the dark [76]; if, however, antioxidants such as hydroquinone or thiophenol are added, the isomerization does not proceed even in sunlight. These inhibitors react rapidly with the free atoms of bromine and with radicals, causing termination of chains [77].

In many cases photochemical isomerization of alkenes may be caused by irradiation without the use of catalysts, by using light of a sufficiently short wavelength to activate the double bonds. In the isomerization of alkenes, catalyzed by radicals, less powerful irradiation is needed than in the case of noncatalytic photochemical isomerization. Thus, for maleic acid the wavelengths necessary for the bromine-catalyzed reaction and for the uncatalyzed reaction are 4,360 Å and 3,310 Å, respectively.

### Radical Addition of Hydrogen Bromide

A study of the addition of hydrogen bromide to unsymmetrical alkenes shows that the direction of the reaction depends on the conditions under which it is performed.

When the reaction is carried out with freshly purified reagents in the absence of oxygen, the addition takes place according to Markovnikov's rule

$$CH_3-CH=CH_2+HBr \longrightarrow CH_3-CHBr-CH_3$$

If the addition takes place in the presence of air or, which is much more effective, in the presence of peroxides (acetyl peroxide, benzoyl peroxide, etc.), a different ("anomalous") reaction occurs:

$$CH_3—CH=CH_2+HBr \longrightarrow CH_3—CH_2—CH_2—Br$$

In the absence of air "anomalous" addition may be caused by photochemical dissociation of small amounts of hydrogen bromide and of other readily dissociated substances (such as aldehydes and ketones).

The introduction of peroxides (generally in amounts of about 1 %) may make the addition go quite contrary to Markovnikov's rule. The order of the reaction of HBr addition to strongly polar molecules of the type of acrylic or cinnamic acid does not change when peroxides are added. On the other hand, the addition of antioxidants (hydroquinone, thiocresol, diphenyl amine) neutralizes the action of peroxides and influences the reaction so that it follows Markovnikov's rule.

Kharasch who discovered the "peroxide effect" [78] demonstrated that it takes place in the case of addition of hydrogen bromide to ethylenic and acetylenic hydrocarbons and to dienes.

The reason for the abnormal addition of hydrogen bromide consists in that in the presence of peroxides this reaction changes from a heterolytic (ionic) to a homolytic (radical) reaction of a chain nature.

The reaction begins with the radical formed on decomposition of the peroxide, attacking a molecule of hydrogen bromide to form atomic bromine:

$$(I)\ CH_3—C(=O)—O—O—C(=O)—CH_3 \longrightarrow CH_3\cdot + CO_2 + \cdot O—COCH_3$$

$$CH_3\cdot + H\!:\!Br \longrightarrow CH_4 + \cdot Br$$

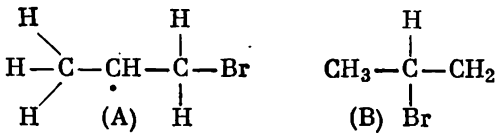
In the second step of the reaction the bromine atom attacks an alkene molecule and adds to the methylene group:

$$(II)\ CH_3—CH=CH_2+\cdot Br \longrightarrow CH_3—CH—CH_2—Br$$

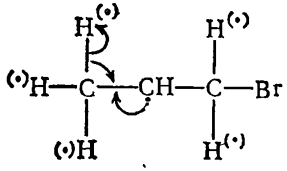
The addition of atomic bromine to the methylene and not the methine group can be explained as follows*: the addition of bromine to the methylene group, on the one hand, and to the methine group,

* The explanation often given in the literature, according to which the bromine atom adds to the methylene group because it is an electrophilic reagent (tending to acquire an extra electron to complete its octet), and therefore should attack at the point of greatest electron density in the molecule, is incorrect (see pages 284-285).

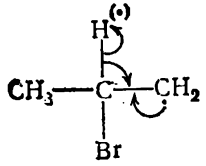
on the other, results in the radicals A and B, respectively.



Of the two radicals, radical A would possess less energy (and would therefore be more stable), because in it the unpaired electron of the carbon atom is conjugated with the σ electrons of five C — H bonds, and therefore not only the carbon, but also the five hydrogen atoms are of a radical nature (the bent arrows indicate the conjugation of the unpaired electrons of the carbon atom with the σ electrons of only one C — H bond of the radical A).

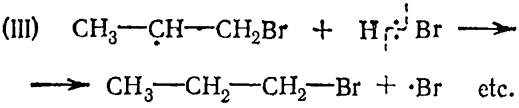


In the radical B the unpaired electron of the carbon atom can be conjugated with the σ electrons of only one C — H bond.



On the strength of this the electron cloud of the unpaired electron is much more localized on the carbon atom and for this reason the energy of radical B is greater than that of radical A.

The third step of hydrogen bromide addition consists in reaction of the radical formed in step II with another hydrogen bromide molecule, resulting in the final product and atomic bromine capable of continuing the chain reaction:



The role of inhibitor-antioxidants is that they react readily with the active radicals ($CH_3^{\bullet}$, $CH_3COO^{\bullet}$, $Br^{\bullet}$, $CH_3\dot{C}HCH_2Br$), forming inactive radicals which are incapable of propagating the chain

reaction, and are capable only of dimerizing

$$R^{\bullet} + H-S-C_6H_5 \longrightarrow R-H + {}^{\bullet}S-C_6H_5$$
$$2\,{}^{\bullet}S-C_6H_5 \longrightarrow C_6H_5-S-S-C_6H_5$$

This results in chain termination and in unfavourable conditions for the radical addition of hydrogen bromide. In such a case, the ionic reaction takes place and the addition proceeds according to Markovnikov's rule.

Investigation of the by-products of the reaction confirmed the radical character of hydrogen bromide addition in the presence of peroxides.

Thus, it was found that hydrogen bromide reacts with stilbene in the dark in the presence of oxygen, forming stilbene dibromide as a by-product; if the reaction is carried out with allyl bromide (under the same conditions) 1,2,3-tribromopropane, hydrogen peroxide and free bromine are formed as by-products of the reaction:

$$C_6H_5-CH=CH-C_6H_5 \xrightarrow{HBr,\ O_2} \begin{cases} \longrightarrow C_6H_5CH_2-CHBr-C_6H_5 \\ \text{Main product} \\ \longrightarrow C_6H_5-CHBr-CHBr-C_6H_5 \\ \text{By-product} \end{cases}$$

$$CH_2=CH-CH_2Br \xrightarrow{HBr,\ O_2} \begin{cases} \longrightarrow CH_2Br-CH_2-CH_2Br \\ \text{Main product} \\ \longrightarrow CH_2Br-CHBr-CH_2Br + H_2O_2 + Br_2 \\ \text{By-product} \end{cases}$$

It is obvious that such by-products cannot form as a result of ionic processes but only as a result of radical reactions.

It is very interesting that the addition of peroxides may change the direction of addition of hydrogen bromide to unsaturated compounds. Peroxides have no influence on the direction of addition of HCl*, HF and HI to unsaturated compounds.

| Reaction | Heat of reaction $\Delta H$, kcal | | | |
|---|---|---|---|---|
| | $x=$ F | Cl | Br | I |
| Step I $R^{\bullet} + HX \rightarrow RH + {}^{\bullet}X$ | −60 | −15 | 0 | +16 |
| Step II $R'-CH=CH_2 + {}^{\bullet}X \rightarrow R'-\dot{C}H-CH_2X$ | +66 | +26 | +13 | −1 |
| Step III $R'-\dot{C}H-CH_2-X + HX \rightarrow R'CH_2CH_2X + {}^{\bullet}X$ | −60 | −15 | 0 | +16 |

This phenomenon becomes understandable if thermochemical data are considered [79].

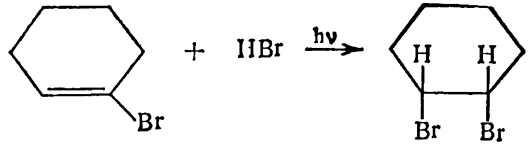
The heats of reactions of the individual steps of radical addition of hydrogen halides to alkenes have the following approximate values.

* For free-radical addition of HCl to alkenes see [30].

It is evident from the table that the total heat effect of the reaction is negative for hydrogen fluoride and hydrogen chloride. Therefore, the energy of activation required to make this process work would be so high that the probability of its realization is very small. In the case of hydrogen iodide, it does not take place despite the positive total heat effect of the radical reaction. The reason for this is the very low activity of the iodine atoms formed in stages I and III; because of this, the competing ionic reaction of HI addition proceeds much faster. It should be also noted that hydrogen iodide is an antioxidant which rapidly destroys peroxide radicals.

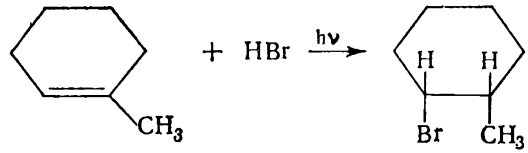
**Stereochemistry of Free-Radical Additions.** The stereochemistry of free-radical addition of HBr cannot be investigated in the case of acyclic unsaturated compounds owing to the reversibility of this reaction and to the rapid *cis-trans*-isomerization of alkene compounds (page 272). In the case of cyclic systems *cis-trans*-isomerization can be avoided and the stereochemistry of the reaction can be established.

Free-radical addition of hydrogen bromide to 1-bromocyclohexene yields *cis*-1,2-dibromocyclohexane exclusively:




It is clear that the reaction proceeds as a *trans*-addition. As *cis*-1,2-dibromocyclohexane is thermodynamically less stable than the *trans*-isomer, the result of the reaction cannot be attributed to another mechanism of the type: *cis*-addition with the formation of a *trans*-isomer → *cis*-isomerization.

The reaction of hydrogen bromide with 1-methylcyclohexene-1* is also a *trans*-addition resulting in *cis*-1-bromo-2-methylcyclohexane.




The radical-chain addition of $BrCCl_3$ to cyclohexene is also a *trans*-addition.

* The addition of HBr to 1-methylcyclohexene-1 is a rare example of ionic and radical additions proceeding at comparable reaction rates. The reaction mechanism depends on the conditions: at −80° the reaction is exclusively heterolytic, at +35° it is exclusively homolytic.

Thus, all *reactions of homolytic addition to the double carbon-carbon bond* which have been studied stereochemically so far *are trans-additions.*

### Addition of Bisulphites and Thiols to Alkenes

For a long time it was accepted that bisulphite additions were characteristic of aldehydes and certain ketones.

It was shown, however, that in the presence of air or peroxides bisulphites add to alkenes. For example, ammonium bisulphite adds to styrene to form ammonium β-phenylethanesulphonate

$$C_6H_5-CH=CH_2+NH_4HSO_3 \longrightarrow C_6H_5-CH_2-CH_2-SO_3NH_4$$

Reactions of this type are sharply inhibited by the addition of antioxidants. It follows that the addition of bisulphites to alkenes is a radical chain reaction proceeding according to the following mechanism [80]:

$$\left[H-O-\underset{\underset{O}{\|}}{\ddot{S}}=O\right]^- + R^\bullet \xrightarrow[\text{(Step I)}]{} \overset{(-)}{R}: + H-O-\underset{\underset{O}{\|}}{\dot{S}}=O$$

or

$$\left[H-O-\underset{\underset{O}{\|}}{\ddot{S}}=O\right]^- + R^\bullet \longrightarrow R-H + \left[O-\underset{\underset{O}{\|}}{\dot{S}}=O\right]^-$$

$$C_6H_5-CH=CH_2+H\dot{S}O_3 \xrightarrow[\text{(Step II)}]{} C_6H_5-\dot{C}H-CH_2SO_3H$$

$$C_6H_5\dot{C}H-CH_2-SO_3H+[HSO_3]^- \xrightarrow[\text{(Step III)}]{} C_6H_5CH_2-CH_2SO_3H+[\dot{S}O_3]^-$$

In step I the initiating radical removes an electron from the bisulphite ion, resulting in a bisulphite radical with an odd electron on the sulphur atom ($H\dot{S}O_3$). The radical formed in step II adds to the methylene group of styrene (cf. page 291). In step III the hydrogen is removed, regenerating the bisulphite radical.

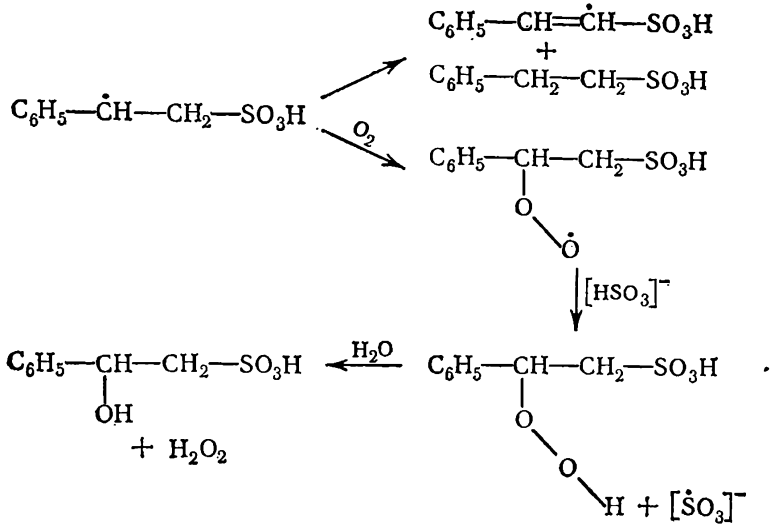
Depending on the acidity of the solution the active radical may be either the electrically neutral molecule with an odd number of electrons ($H\dot{S}O_3$) or the radical ion $(\dot{S}O_3)^-$:

$$(\dot{S}O_3)^- + H_2O \rightleftarrows H\dot{S}O_3 + OH^-$$

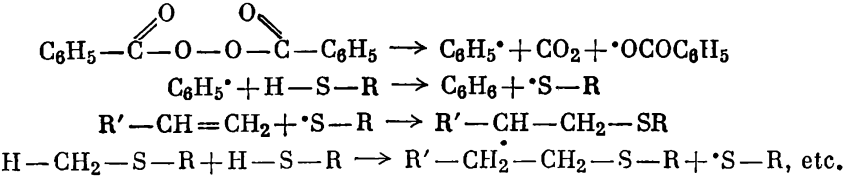
These substances are also important in the autoxidation of sulphites to sulphates.

Among the by-processes involved in the addition of bisulphites to alkenes are disproportionation and oxidation (by air) of the

intermediate hydrocarbon radicals, e.g.:

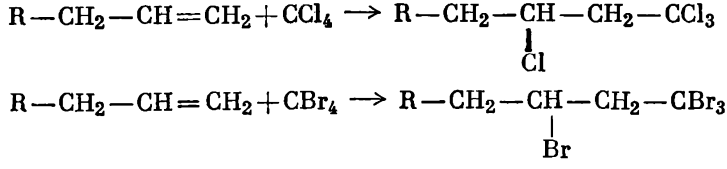


In the absence of catalysts thiols do not add to alkenes. In the presence of peroxides or if the reaction mixture is irradiated with ultraviolet light, mercaptans, thioethers and hydrogen sulphide may add to alkenes. The addition takes place contrary to Markovnikov's rule and is a radical chain process. The mechanism of this reaction may be illustrated by the following schemes:



### Radical Addition of Halogen Derivatives to Alkenes

In the presence of peroxides or on irradiation of the reaction mixture by ultraviolet light polyhalomethanes such as carbon tetrachloride, chloroform, carbon tetrabromide, bromoform, bromotrichloromethane, add to alkenes.



$$R-CH_2-CH=CH_2+CHCl_3 \longrightarrow R-CH_2-CH_2-CH_2-CCl_3$$

$$R-CH_2-CH=CH_2+CHBr_3 \longrightarrow R-CH_2-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_2-CHBr_2$$

$$R-CH_2-CH=CH_2+BrCCl_3 \longrightarrow R-CH_2-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_2-CCl_3$$

Bromoacetic ester adds under analogous conditions:

$$R-CH_2-CH=CH_2+Br-CH_2-COOC_2H_5 \longrightarrow$$
$$\longrightarrow R-CH_2-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_2-CH_2-COOC_2H_5$$

These reactions proceed better in the absence of air, because the latter is an inhibitor.

All these reactions are radical chain processes. For example, the addition of carbon tetrachloride in the presence of organic peroxides or when irradiated with ultraviolet light proceeds according to the following scheme [81]:

$$CCl_4 \xrightarrow{h\nu} Cl^{\bullet}+{}^{\bullet}CCl_3$$

$$R-CH_2-CH=CH_2+{}^{\bullet}CCl_3 \longrightarrow R-CH_2-\overset{\displaystyle \bullet}{\underset{|}{CH}}-CH_2-CCl_3$$

$$R-CH_2-\overset{\displaystyle \bullet}{\underset{|}{CH}}-CH_2-CCl_3+CCl_4 \longrightarrow R-CH_2-\underset{\displaystyle Cl}{\underset{|}{CH}}-CH_2-CCl_3+{}^{\bullet}CCl_3, \text{ etc.}$$

A study of the products formed suggested that the homolytic break occurs the most readily at the C — Br bond ($CHBr_3$ adds to alkenes even under exposure to visible light), with greater difficulty at the C — H bond and with still more difficulty at the C—Cl bond.

In the presence of acetyl or benzoyl peroxide free-radical addition of phosphorus trichloride to alkenes can be accomplished [82]:

$$CH_3-\overset{\displaystyle O}{\overset{\|}{C}}-O-O-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3 \longrightarrow CH_3^{\bullet}+CO_2+{}^{\bullet}OCOCH_3$$

$$CH_3^{\bullet}+PCl_3 \longrightarrow CH_3Cl+{}^{\bullet}PCl_2$$

$$R-CH_2-CH=CH_2+{}^{\bullet}PCl_2 \longrightarrow R-CH_2-\overset{\displaystyle \bullet}{\underset{|}{CH}}-CH_2-PCl_2$$

$$R-CH_2-\overset{\displaystyle \bullet}{\underset{|}{CH}}-CH_2-PCl_2+PCl_3 \longrightarrow R-CH_2-\underset{\displaystyle Cl}{\underset{|}{CH}}-CH_2-PCl_2+{}^{\bullet}PCl_2, \text{ etc.}$$

Finally, it was found possible to add silicochloroform to ethylenic [83] and acetylenic [84] hydrocarbons in the presence of peroxides

or ultraviolet light:

$$(CH_3COO)_2 \longrightarrow CH_3^{\bullet} + CO_2 + {}^{\bullet}OCOCH_3$$

$$CH_3^{\bullet} + H-SiCl_3 \longrightarrow CH_4 + {}^{\bullet}SiCl_3$$

$$R-CH_2-CH=CH_2 + {}^{\bullet}SiCl_3 \longrightarrow R-CH_2-\dot{C}H-CH_2-SiCl_3$$

$$R-CH_2-\dot{C}H-CH_2-SiCl_3 + H-SiCl_3 \longrightarrow$$

$$\longrightarrow R-CH_2-CH_2-CH_2-SiCl_3 + {}^{\bullet}SiCl_3 \text{ etc.}$$

**Addition of Alcohols, Aldehydes and Ketones**

Primary and secondary alcohols add to alkenes in the presence of *tert*-butyl peroxide or upon irradiation. This gives rise to the corresponding secondary or tertiary alcohols and to telomerization products [85] (page 302).

For example, the reaction of ethyl alcohol with ethylene results in butanol-2, hexanol-2, octanol-2 and decanol-2.

The reaction proceeds according to the schemes:

$$(CH_3)_3C-O:O-C(CH_3)_3 \longrightarrow 2(CH_3)_3C-O^{\bullet}$$

$$(CH_3)_3C-O^{\bullet} + CH_3CH_2OH \longrightarrow (CH_3)_3COH + CH_3-\dot{C}H-OH$$

$$CH_3-\dot{C}H-OH + CH_2=CH_2 \longrightarrow$$

$$\longrightarrow CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-CH_2^{\bullet}$$

$$\xrightarrow{CH_3CH_2OH} CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2CH_3 + CH_3-\dot{C}H-OH$$

$$\xrightarrow{CH_2=CH_2} CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-CH_2-CH_2-CH_2^{\bullet}$$

etc.

$$\xrightarrow{CH_3CH_2OH} \xrightarrow{CH_2=CH_2}$$

etc.

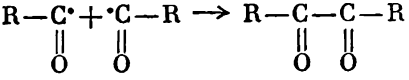
Aldehydes [86] and ketones [87] add to alkenes under analogous conditions:

$$R-CHO \xrightarrow{h\nu} R-\dot{C}=O + {}^{\bullet}H$$

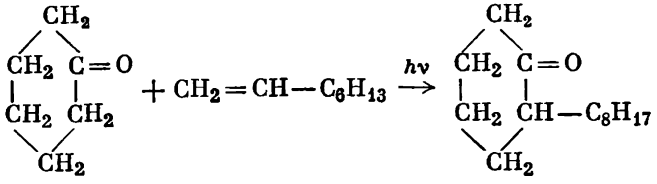
$$R-\dot{C}=O + R'-CH=CH_2 \longrightarrow R-\underset{\displaystyle O}{\underset{\|}{C}}-CH_2-\dot{C}H-R'$$

$$R-\underset{\displaystyle O}{\underset{\|}{C}}-CH_2-\dot{C}H-R' + R-CHO \longrightarrow R-\underset{\displaystyle O}{\underset{\|}{C}}-CH_2-CH_2-R' + R-\dot{C}=O \text{ etc.}$$

α-Diketones are formed as a result of a side reaction (involving chain termination):



Cyclohexanone adds to octene-1 forming 2-octylcyclohexanone:



**Direction of Reactions of Radical Addition**

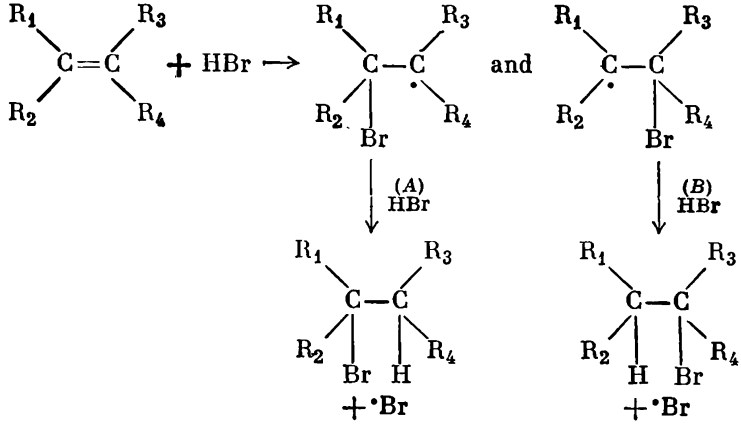
The direction of addition of free radicals to double bonds depends on the nature of the atoms or groups of atoms linked to both unsaturated carbon atoms.

Three hypotheses have been put forward regarding the factors determining the direction of free-radical addition to the carbon-carbon double bond [88]:

(a) halogen atoms and certain other free radicals are electrophilic agents and consequently attack the area of greatest electron density of the unsaturated compound (e.g., the methylene group in the propylene molecule $CH_3 - \overset{\delta\oplus}{C}H = \overset{\delta\ominus}{C}H_2$);

(b) the point of attack of an alkene by a free radical depends on steric factors;

(c) the point of attack depends on the relative stability of the two possible intermediate radicals, formed after addition of the free radical to the double bond, for example:



The reaction proceeds in the direction which yields the most stable radical (A or B) possessing the least energy.

The first hypothesis was proposed by Waters, the latter two by Mayo and Walling.

Recently Haszeldine obtained some interesting results permitting a better evaluation of the three hypotheses.

Trifluoroiodomethane adds to alkenes when irradiated with ultraviolet light, the first step consisting of addition of the trifluoromethyl radical $CF_3^{\cdot}$.

For a large number of unsaturated compounds $R-CH=CH_2$ ($R=CH_3$, Cl, F, $COOCH_3$, $CF_3$, CN) the reaction proceeds in such a way that the radical $^{\cdot}CF_3$ adds exclusively to the methylene group [89]:

$$R-CH=CH_2+CF_3-I \xrightarrow{h\nu} R-\underset{I}{CH}-\underset{CF_3}{CH_2}$$

However, the nature of polarization of the double bond in unsaturated compounds of this type is different. If, for example, in propylene the methylene group is the seat of greatest electron density $R-\overset{\delta+}{C}H=\overset{\delta-}{C}H_2$ ($R=CH_3$), in acrylonitrile, 1,1,1-trifluoropropylene, etc., the methylene group has a lower electron density than the methine group:

$$R-\overset{\delta-}{C}H=\overset{\delta+}{C}H_2 \quad (R=CN,\ CF_3,\ \text{etc.})$$

A study of addition reactions of perfluoropropylene has confirmed that free radicals (and even halogen atoms) do not necessarily attack the seat of greatest electron density [90].

The perfluoropropylene molecule is polarized as follows: $CF_3-\overset{\delta-}{C}F=\overset{\delta+}{C}F_2$. This follows from the direction of the ionic addition of hydrogen bromide:

$$CF_3-CF=CF_2+H^+Br^- \longrightarrow CF_3-\underset{H}{CF}-\underset{Br}{CF_2}$$

In the photochemical addition of $ICF_3$ and HBr to perfluoropropylene the radical $^{\cdot}CF_3$ and atomic bromine $^{\cdot}Br$ attack the group $CF_2$ exclusively, this being the point of lowest electron density.

The above examples of the direction of addition in free-radical reactions could be attributed to the influence of steric factors (hypothesis *b*). However, the latter apparently cannot play the decisive role in this case.

Even the reaction

$$CF_2Br_2 \xrightarrow{h\nu} {}^{\bullet}CF_2Br + {}^{\bullet}Br$$

$$CH_3-CF=CH-CH_3 \xrightarrow{{}^{\bullet}CF_2Br} CH_3-\dot{C}F-\underset{\displaystyle CF_2+Br}{\underset{|}{CH}}-CH_3 \xrightarrow{CF_2Br_2}$$

$$\longrightarrow CH_3-\underset{\displaystyle Br}{\underset{|}{CF}}-\underset{\displaystyle CF_2Br}{\underset{|}{CH}}-CH_3 + {}^{\bullet}CF_2-Br, \text{ etc.}$$

can hardly be understood if only steric hindrance is considered, because fluorine is but slightly larger in volume than hydrogen.

Quite incomprehensible from this point of view is the nature of addition of the radicals $^{\bullet}CF_3$ and $^{\bullet}CCl_3$ to 1,1-difluoropropene-1.

$$CH_3-CH=CF_2$$
$$R^{\bullet}\nearrow$$

The addition takes place at the methine group though the latter is sterically more inhibited than the terminal $CF_2$ group.

*The decisive factor in the orientation of homolytic addition to the carbon-carbon double bond is evidently the relative stability of the two intermediate radicals (hypothesis c).*

Unfortunately, so far there is no general method of evaluating the relative stability of free radicals; in the majority of cases semi-empirical methods are used for this purpose (page 274).

### Addition of Alkali Metals to Alkenes

Alkali metals are capable of adding to the carbon-carbon double bond if the latter is activated by conjugation with an aromatic ring or by some similar group of atoms.

Three types of addition of alkali metals to double bonds are known: "normal", "dimerizing" and "disproportionating" [91].

*"Normal" addition*

$$C_6H_5-CH=CH-C_6H_5 + 2M \longrightarrow C_6H_5-\underset{\displaystyle M}{\underset{|}{CH}}-\underset{\displaystyle M}{\underset{|}{CH}}-C_6H_5; \quad M = Li, K, Na$$

*"Dimerizing" addition*

$$2(C_6H_5)_2C=CH_2 + 2M \longrightarrow (C_6H_5)_2\underset{\displaystyle M}{\underset{|}{C}}-CH_2CH_2-\underset{\displaystyle M}{\underset{|}{C}}(C_6H_5)_2$$

*"Disproportionating" addition*

$$2(C_6H_5)_2C{=}CHCH_2C_6H_5 + 2M \longrightarrow$$

$$\longrightarrow (C_6H_5)_2C(M)-CH_2CH_2-C_6H_5 + (C_6H_5)_2C(M)-CH{=}CH-C_6H_5$$

All three types of additions of alkali metals to unsaturated aromatic compounds may be thought of as a result of either homolytic or heterolytic transformations.

If the reactions proceed through homolytic processes, their mechanism may be represented by the following schemes:

*"Normal" addition*

$$C_6H_5-CH{=}CH-C_6H_5 + {\cdot}M \longrightarrow C_6H_5-\dot{C}H-CH(M)-C_6H_5 \xrightarrow{{\cdot}M}$$

$$\longrightarrow C_6H_5-CH(M)-CH(M)-C_6H_5$$

*"Dimerizing" addition*

$$(C_6H_5)_2C{=}CH_2 + {\cdot}M \longrightarrow (C_6H_5)_2C(M)-\dot{C}H_2$$

$$2(C_6H_5)_2C(M)-\dot{C}H_2 \longrightarrow (C_6H_5)_2C(M)-CH_2-CH_2-C(M)(C_6H_5)_2$$

*"Disproportionating" addition*

$$(C_6H_5)_2C{=}CHCH_2C_6H_5 + {\cdot}M \longrightarrow (C_6H_5)_2C(M)-\dot{C}H-CH_2-C_6H_5$$

$$2(C_6H_5)_2C(M)-\dot{C}H-CH_2C_6H_5 \longrightarrow$$

$$\longrightarrow (C_6H_5)_2C(M)-CH_2-CH_2-C_6H_5 + (C_6H_5)_2C(M)-CH{=}CH-C_6H_5$$

It should be pointed out, however, that the initial addition of an alkali metal atom to the least hydrogenated carbon atom of diphenylethylene and triphenylpropylene in "dimerizing" and correspondingly in "disproportionating" addition is improbable because the resulting free radicals must possess comparatively large energies (page 291).

Therefore, it is more probable that "dimerizing" and "disproportionating" additions consist of mixed processes: homolytic "normal" addition takes place first, and then the organometallic compounds formed give the end products as a result of secondary heterolytic transformations (pages 294-295).

In such a case the mechanism of "dimerizing" and "disproportionating" additions may be represented as follows:

*"Dimerizing" addition*

$$(C_6H_5)_2C{=}CH_2 \xrightarrow{\cdot M} (C_6H_5)_2\dot{C}{-}CH_2{-}M \xrightarrow{\cdot M} (C_6H_5)_2C(M){-}CH_2{-}M \xrightarrow{(C_6H_5)_2C=CH_2}$$

$$\longrightarrow (C_6H_5)_2C(M){-}CH_2{-}CH_2{-}C(M)(C_6H_5)_2$$

*"Disproportionating" addition*

$$(C_6H_5)_2C{=}CHCH_2C_6H_5 \xrightarrow{M\cdot} (C_6H_5)_2\dot{C}{-}CH(M){-}CH_2C_6H_5 \xrightarrow{M\cdot}$$

$$\longrightarrow (C_6H_5)_2C(M){-}CH(M){-}CH_2C_6H_5 \xrightarrow{(C_6H_5)_2C=CHCH_2C_6H_5}$$

$$\longrightarrow (C_6H_5)_2C(M){-}CH_2CH_2C_6H_5 + (C_6H_5)_2C(M){-}CH{=}CH{-}C_6H_5$$

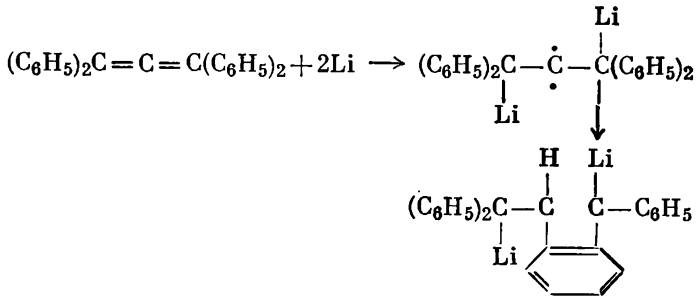
Exact determination of the mechanism of the reactions of alkenes with alkali metals, which are on the borderline between homolytic and heterolytic processes, requires additional detailed research with the use of physicochemical methods.

According to Schlenk and Bergmann [92] the addition of alkali metals to allenic hydrocarbons proceeds through the intermediate formation of a biradical. Thus, the reaction of tetraphenyl allene with metallic sodium is represented as follows:

$$(C_6H_5)_2C{=}C{=}C(C_6H_5)_2 \xrightarrow{2Na} (C_6H_5)_2C(Na){-}\dot{C}{-}C(Na)(C_6H_5)_2 \longrightarrow$$

$$\longrightarrow (C_6H_5)_2C(Na){-}C{=}C(C_6H_5)_2 \xrightarrow{H_2O} (C_6H_5)_2CH{-}CH{=}C(C_6H_5)_2$$

The addition of lithium to tetraphenyl allene proceeds differently aud results in a cyclic compound:



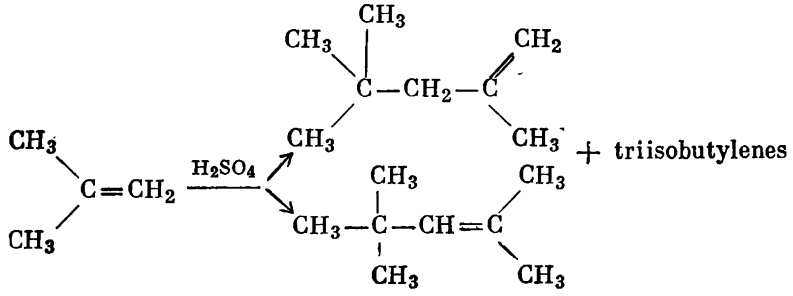
It is possible that aliphatic alkenes are also capable of homolytic addition to metals, because metals such as sodium are good polymerization catalysts for alkenes (page 294).

## 4-1.4 Polymerization of Alkenes

Polymerization of alkenes is a process of utmost importance. This reaction is the basis of large-scale industrial processes such as production of synthetic rubber, various types of plastics and synthetic fibres.

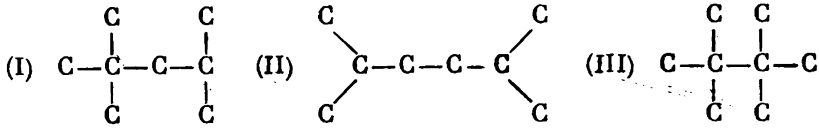
### Mechanism of Polymerization of Isobutylene

Polymerization of alkenes was first discovered and studied by Butlerov in his work on isobutylene [93]. But Butlerov showed that when isobutylene was polymerized under the action of sulphuric acid, a mixture of two diisobutylenes and also triisobutylenes were formed:



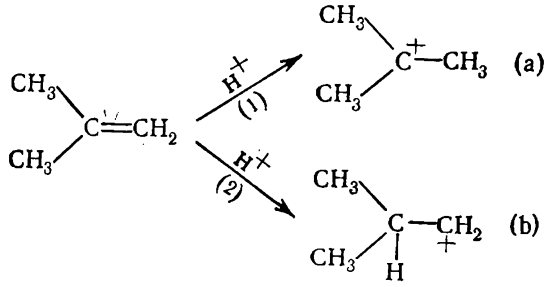
Polymers of higher molecular weights are also formed in small quantities.

Formally, dimerization of isobutylene may result in any hydrocarbon possessing one of the following three carbon skeletons:

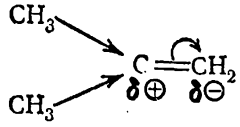



Actually, only diisobutylenes possessing the carbon skeleton I are formed. This may be explained as follows.

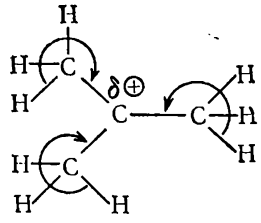
Polymerization of isobutylene starts with the addition of a proton (from sulphuric acid) to the alkene molecule. The proton may add either to the carbon atom of the methylene group or to the central carbon atom




Obviously, reaction (1) would proceed much faster than reaction (2). This follows, first of all, from the nature of polymerization of the double bond of isobutylene:

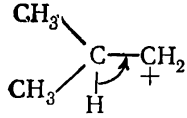


Since the point of greatest electron density in the non-reacting molecule is the carbon of the methylene group, the approach of a proton $H^+$ to it is facilitated. On the other hand, of the two intermediate cations (*a*) and (*b*), cation (*a*) possesses less energy because in it the positive charge may be partly neutralized by a shift of the $\sigma$-electrons of the nine C — H bonds:



Such great possibilities of conjugation cause the central carbon atom to carry only a partial positive charge (all nine hydrogen atoms become positively charged to a small extent).

Cation (*b*) possesses much smaller possibilities for conjugation — the σ-electrons of only one of its C — H bonds can be shifted toward the positively charged carbon atom:

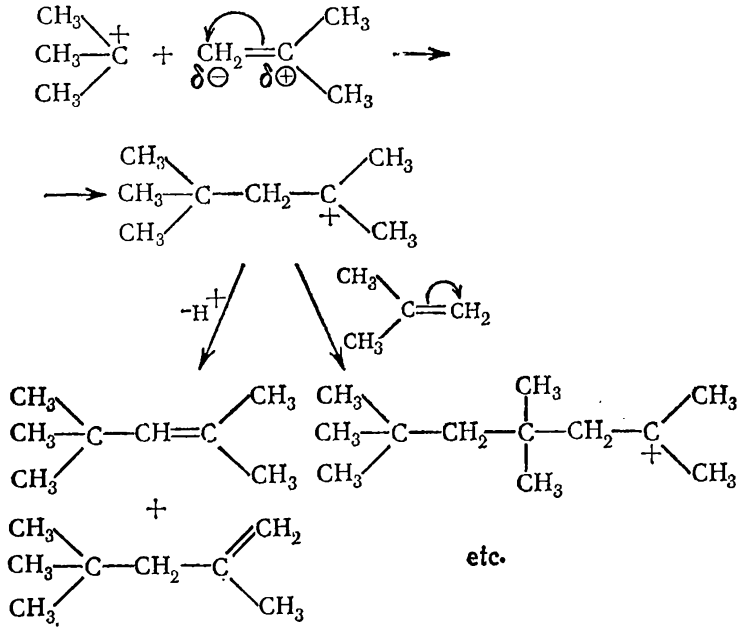


As a result of this the positive charge is localized almost entirely on the carbon atom of the methylene group, so that the energy of cation (*b*) is higher than that of cation (*a*).

Thus both static and dynamic factors favour the addition of proton to the methylene group.

The resulting cation $(CH_3)_3C^+$ adds to the methylene group of the second isobutylene molecule.

The cation formed in this operation may react with another molecule of isobutylene forming a triisobutylene cation, or splitting off a proton to give one of the two isomeric diisobutylenes:



Polymerization of isobutylene occurs not only under the influence of sulphuric acid but also under the action of other electrophilic reagents (zinc chloride, boron trifluoride, etc.). The reaction mechanism is quite similar in all cases.

### Mechanism of Styrene Polymerization

Interesting relationships were established in a study of styrene polymerization initiated by electrophilic, radical and nucleophilic reagents.

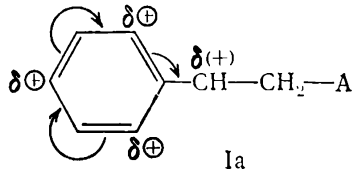
Theoretical examination of the question shows that the polymerization of styrene is independent of the nature of the reagent and must be initiated by addition of the reagent to the methylene group of the styrene molecule:

$$\text{I}\quad C_6H_5-CH=CH_2+\overset{+}{A} \longrightarrow C_6H_5-\overset{+}{C}H-CH_2-A$$

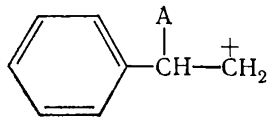
$$\text{II}\quad C_6H_5-CH=CH_2+:B^- \longrightarrow C_6H_5-\overset{(-)}{\underset{\cdot\cdot}{C}}H-CH_2-B$$

$$\text{III}\quad C_6H_5-CH=CH_2+{}^{\bullet}R \longrightarrow C_6H_5-CH-CH_2-R$$

This, at first glance, unexpected conclusion follows from a comparative evaluation of the energy of the respective ions and radicals, which may form when the reagent adds to the methylene group, on the one hand, and to the methine group, on the other. In the reaction of styrene with the electrophilic reagent $A^+$ two ions of the following structure may form:




Ia

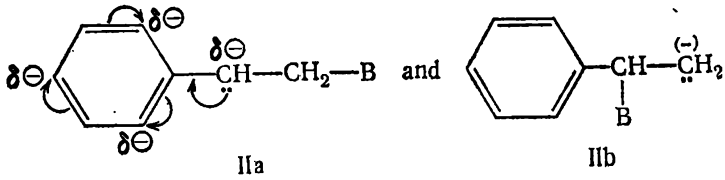



Ib

Their energies differ, however. In cation Ia the $\pi$ electrons of the benzene ring are displaced towards its positively charged $\alpha$-carbon atom. As a result of this, the $\alpha$-carbon atom does not possess a fully localized positive charge; in their turn the ortho- and para-carbon atoms of the benzene ring carry partial positive charges. In cation Ib the $\pi$ electrons of the benzene ring cannot participate in the "extinction" of the positive charge on the $\beta$-carbon atom. Owing to the localized charge on the $\beta$-carbon atom the energy of the Ib cation is greater than that of the Ia cation.

Obviously the cation Ia must form more rapidly. In other words, electrophilic reagents would add to the methylene group of styrene.

In the reaction of styrene with a nucleophilic reagent $B^-$ two anions may result:

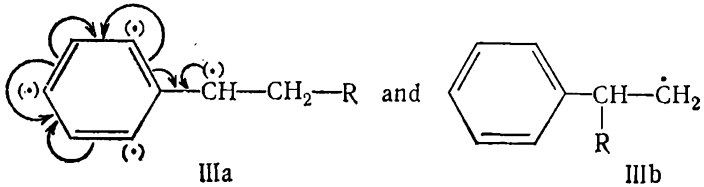



IIa IIb

In anion IIa the free electron pair of the α-carbon atom reacts with the π electrons of the benzene ring. This pair is not localized on the α-carbon atom, but is displaced toward the benzene ring. As a result, the cloud density of this electron pair is distributed among the α-carbon atom, two ortho-carbon atoms and one para-carbon atom of the benzene ring, which carry a certain small negative charge. In anion IIb the electron pair of the β-carbon atom cannot interact with the π electron of the benzene ring. Therefore the β-carbon atom carries a localized negative charge, owing to which the energy of the IIb anion is higher than that of the IIa anion.

Therefore, when a nucleophilic reagent reacts with the styrene molecule the reagent must also add to the methylene group.

When a radical reagent R· adds to the styrene molecule, two intermediate radicals may form:




IIIa IIIb

In radical III*a* the unpaired electron of the α-carbon atom interacts with the π electrons of the benzene ring (page 340). The cloud of the odd electron is distributed among the α-carbon atom and three carbon atoms of the benzene ring (ortho- and para-atoms) and consequently the α-carbon atom has no localized electron.

In radical III*b* interaction between the unpaired electron of the β-carbon atom and the π electrons of the benzene ring is impossible, as a result of which the β-carbon atom carries a localized electron. For this reason the III*b* radical possesses more energy than the III*a* radical.

Thus, radical reagents must also add to the methylene group of the styrene molecule.

Experimental data are in complete agreement with the above deductions, according to which any reagent attacks styrene at the methylene group.

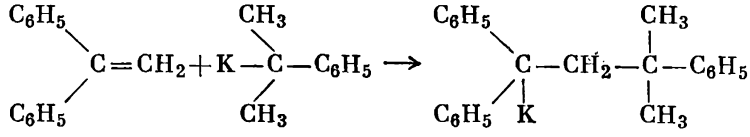
In electrophilic addition of hydrogen halides to styrene (as was shown earlier on page 214, the first stage of the reaction consists in addition of hydrogen ion $H^+$) hydrogen adds to the methylene group:

$$C_6H_5-CH=CH_2+H^+Br^- \longrightarrow C_6H_5-\underset{Br}{CH}-\underset{H}{CH_2}$$

In the radical addition of hydrogen bromide to styrene in the presence of peroxides (the reaction is initiated by the addition of atomic bromine to the double bond [page 274]) bromine adds to the methylene group:

$$C_6H_5-CH=CH_2+HBr \xrightarrow{\text{Peroxides}} C_6H_5-\underset{H}{CH}-\underset{Br}{CH_2}$$

There is no experimental evidence concerning nucleophilic addition to styrene because nucleophilic reagents generally cause polymerization of styrene. However, reactions are known, for example, the addition of the potassium derivative of isopropylbenzene to unsymmetrical diphenylethylene (which undoubtedly starts with an attack by the organic anion), in which the anion (phenyl isopropyl anion) adds also to the methylene group:



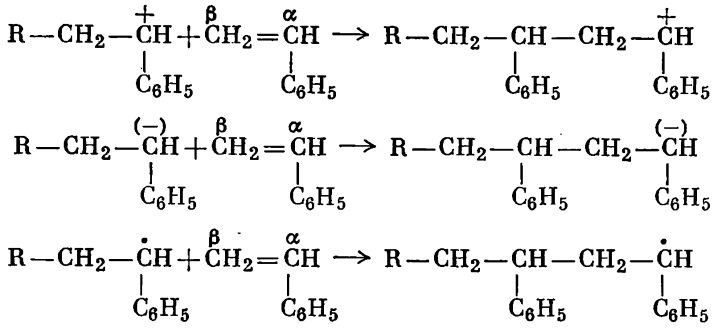
Taking the above discussion into consideration, all three types of reagents should give the same type of polymerization of styrene.

Designating by R electrophilic (such as $SnCl_4$), nucleophilic [such as $(C_6H_5)_3C^-Na^+$] and radical (such as $C_6H_5^{\cdot}$) reagents for styrene polymerization, the structure of the products formed when R adds to styrene is as follows:

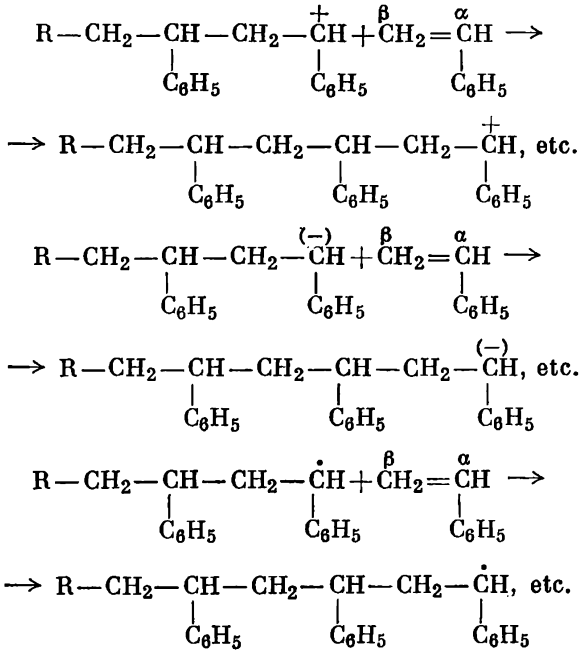
$$R-CH_2-\overset{+}{C}H-C_6H_5, \quad R-CH_2-\overset{(-)}{C}H-C_6H_5 \quad \text{and} \quad R-CH_2-\overset{\cdot}{C}H-C_6H_5$$

I II III

For the reasons given above the next styrene molecule may add to cation I, anion II and radical III only through its methylene group:



Further growth of the chain must proceed quite analogously:



Therefore, independently of the nature of the reagent causing polymerization, chain growth proceeds by the addition of the methylene group of one styrene molecule to the methine group of another molecule ($\alpha$, $\beta$).

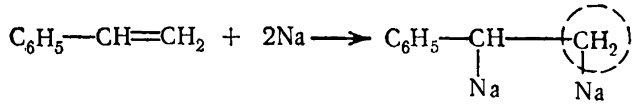
This conclusion agrees satisfactorily with the data obtained in investigating the structure of styrene polymers.

Polymerization of styrene under the influence of metallic sodium proceeds in an interesting manner.

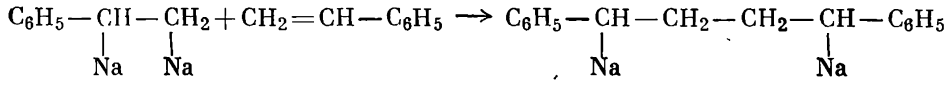
If the reaction stops at the stage of dimerization (as it does when sodium acts on styrene in alcoholic solution), the result is 1,4-diphenylbutane, the formation of which cannot be imagined otherwise than as a result of dimerization of styrene at the β-carbon atom (β, β). If the polymerization proceeds further, with the formation of polystyrenes, the predominant molecular configuration is the configuration α, β.

Generally polymerization of unsaturated compounds by alkali metals is considered a radical reaction; however, free-radical reactions cannot account for the above peculiarities of styrene polymerization. These peculiarities become understandable if styrene polymerization under the influence of metallic sodium is assumed to follow an organometallic mechanism.

In such a case the first stage of the reaction consists in addition of two sodium atoms to the double bond:



In the disodium derivative of styrene the site of highest nucleophilic activity is the $CH_2$ group*. Therefore, further reaction occurs only between the methylene group of the disodium derivative of styrene and the methylene group of styrene (β, β).



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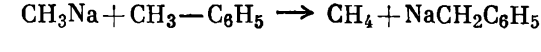
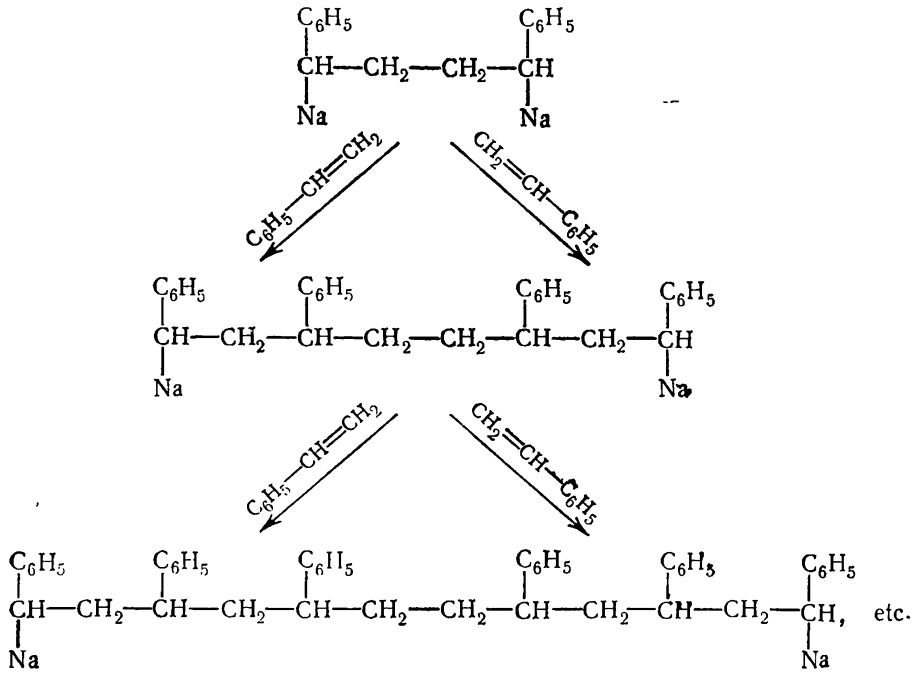
* This conclusion is based on the fact that aliphatic organosodium compounds react readily with toluene, exchanging the proton of the methyl group for sodium, e.g.:

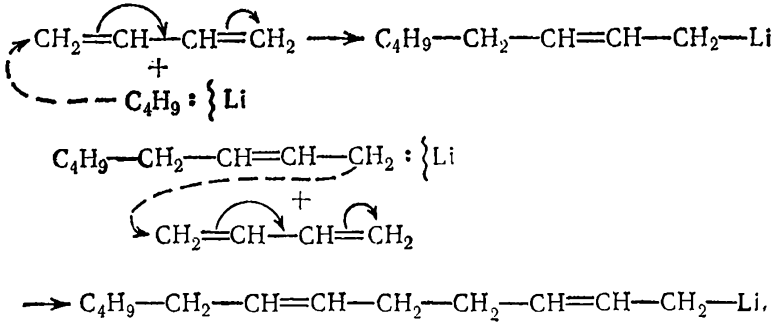


The reverse reaction is impossible because benzylsodium is an insufficiently strong nucleophilic reagent to remove a proton from methane. In disodium-styrene the —CHNa— group is similar in nucleophilic properties to the $NaCH_2$ group in benzylsodium, and the $—CH_2—Na$ group resembles the same group in methylsodium.

If the conditions of the reaction favour further polymerization, growth must occur at both ends (α, β):



The above concept of the organometallic mechanism of styrene polymerization has a sufficiently solid experimental basis because unsaturated hydrocarbons polymerize readily under the influence of known organometallic compounds of alkali metals, e.g.:

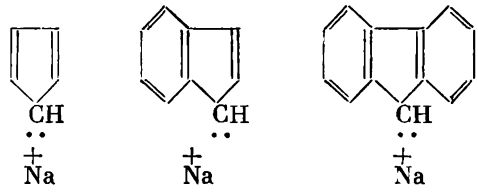


The ratio of 1,4- to 1,2-addition products depends on factors similar to those discussed in connection with electrophilic addition to hydrocarbons with conjugated bonds (page 247).

Since the addition of an organometallic compound RMe to a diene apparently begins with the addition of the anion R:, the nature of the latter largely determines the rate of polymerization.

The most active polymerizing agents of this type are organometallic compounds of alkali metals of the aliphatic series. This is because in the anions of such compounds ($CH_3$:, $C_2H_5$:, $C_3H_7$:, etc.) the electron pair is localized on one carbon atom, and therefore they possess greater energy and high reactivity.

On the contrary, the lithium or sodium derivatives of cyclopentadiene, indene or fluorene are incapable of causing butadiene polymerization, because in the anions of these compounds the electron pair responsible for their negative charge is not localized on any particular carbon atom but is spread over several,



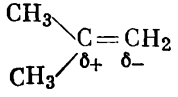

so that these anions possess low energy and low reactivity.

### Effect of Structure on Polymerizability of Alkenes

It is important to consider the effect of the structure of unsaturated hydrocarbons on their ability to polymerize.

When polymerization proceeds under the influence of electrophilic or nucleophilic reagents (heterolytic polymerization), the main part is played by the polarization and polarizability of the double bonds of unsaturated hydrocarbons.

Hydrocarbons with polarized double bonds, such as isobutylene,




polymerize easily. On the other hand, hydrocarbons such as butadiene also polymerize very readily though they have no dipole moment. In these cases easy polymerization is due to the ready polarizability of conjugated bonds under the influence of an attacking reagent.

Sometimes, as, for example, in the case of styrene, the ease of polymerization is due both to polarization and to polarizability.

When the double bonds of unsaturated compounds are not polarized and are difficult to polarize, polymerization takes place only under stringent conditions.

This becomes apparent if the conditions of polymerization of isobutylene and ethylene are compared.

Under the influence of dilute sulphuric acid (65-70%) isobutylene polymerizes at 25-30°.

Aluminium chloride, boron trifluoride and some other similar catalysts cause polymerization of isobutylene (to form a rubber-like polymer) at about —70°.

In the presence of floridine (aluminium hydrosilicate) isobutylene polymerizes readily even at —80°.

Ethylene does not polymerize under the action of sulphuric acid (stable acid and neutral ethyl sulphates result). Attempts to achieve polymerization by raising the temperature were a failure (they resulted only in oxidation of the ethylene).

Ethylene polymerizes under the influence of aluminium chloride or boron trichloride at room temperature and high pressures in the presence of hydrogen chloride as a promoter. However, this causes conjugated polymerization*, yielding a mixture of paraffins and cycloparaffins.

Butlerov was the first to describe the difference between the polymerizability of ethylene, on the one hand, and propylene and butylene, on the other hand, under the influence of boron trifluoride [93]. He showed that in the presence of boron trifluoride ethylene does not polymerize even at 200° while propylene and butylene polymerize at room temperature.

Unsaturated hydrocarbons with unpolarized double bonds that are difficult to polarize may be successfully polymerized in the presence of catalysts of a radical nature, such as organic peroxides. The absence of partial charges does not prevent electrically neutral radicals from attacking the alkenes.

Thus, ethylene when acted upon by peroxides at a pressure of 200 to 300 atm yields a high molecular weight polymer. In the presence of methanol and benzoyl peroxide at 110-120° a wax with a molecular weight ranging from 2,000 to 3,000 is formed. Polymerization taking place at a pressure of 1,000-2,000 atm at 180-220° in the presence of 0.05-0.1 per cent of oxygen (as a catalyst of a radical nature) gives a solid polyethylene (polythene) the molecular weight of which is in the range of 15,000-20,000 and over (up to

---

* It is the custom to distinguish between true and conjugated polymerization. The products of true polymerization are alkenes, the molecular weights of which are multiples of the molecular weight of the monomer. Conjugated polymerization yields a complex mixture of alkanes, alkenes, dienes, cycloalkanes, cycloalkenes, cyclodialkenes, and sometimes aromatic hydrocarbons. The number of carbon atoms in its products are not necessarily divisible by the number of carbon atoms in the monomer.

$\sim$ 50,000). This material possesses exclusively important electrical properties.

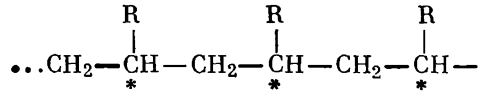
This is known as "high-pressure" polyethylene. Its molecules possess long and short side chains.

Ziegler [94] proposed a method of preparing "low-pressure" polyethylene with a molecular weight of approximately $3 \times 10^6$. His method consists in polymerizing ethylene with the aid of mixed catalysts [for example, $TiCl_4 + Al(C_2H_5)_3$].[1] Titanium is transformed into a compound with a lower valence. Natta proposed an anionic mechanism for this reaction.

Besides being of a higher molecular weight "low-pressure" polyethylene also features a lack of branching in its molecules.

### Stereoregular Polymerization[2]

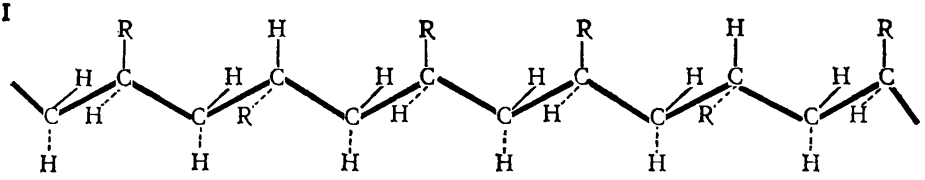
In the polymerization of vinyl compounds of the type $R - CH = CH_2$ compounds of high molecular weight are formed in the polymeric chain of which the carbon atoms linked with the R groups are asymmetric



These atoms are equally likely to form *D*- and *L*-configurations in the course of polymerization; therefore the polymer molecule as a whole should be optically inactive because of statistical intramolecular compensation.

If *D*- and *L*-configurations alternate chaotically in such a molecule, the polymer is called *atactic*.

I



Atactic vinyl polymer

Any order of alternation of the carbon atoms with *L*- and *D*-configurations, no matter how complex, is a characteristic indication of stereoregular polymers.

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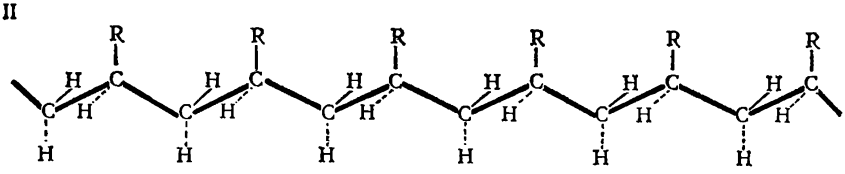
[1] Nenitzescu accomplished polymerization of ethylene at atmospheric pressure using $R—Na + TiCl_4$ as catalyst [95].

[2] See [96] for review.

Stereoregular polymers were synthesized, with asymmetric carbon atoms having the same configuration (*D* or *L*). Such polymers are called *isotactic*.

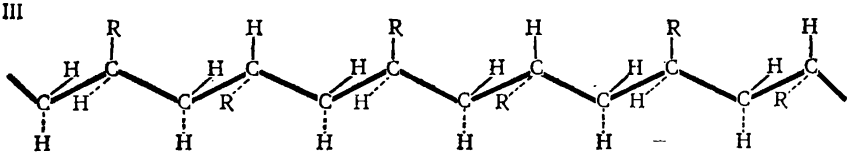
II



Isotactic vinyl polymer

On the other hand, stereoregular polymers were obtained with regular alternation of asymmetric carbon atoms in their molecules (*DL*, *DL*, *DL*...). Such polymers are called *syndiotactic*.

III



Syndiotactic vinyl polymer

Atactic polymers are amorphous, isotactic and syndiotactic are crystalline, therefore the configuration of their chains can be established by X-ray diffraction. Many commercially valuable properties of isotactic and syndiotactic polymers are due to their crystallinity.

To realize stereospecific polymerization it is necessary to control the initiation reaction, the addition reaction and the nature of approach of the monomer to the growing chain [97]. According to Natta [98], stereospecific polymerization of vinyl compounds demands such a control over the process as to make the reaction proceed:

(a) always "head to tail";

(b) without formation of branches due to chain transfer;

(c) without branch formation in the copolymerization of the monomer with oligomers, and

(d) in such a manner that the monomer links themselves form well-ordered spatial configurations.

Essentially, the main problem is to form a transient complex of definite structure at the instant of chain growth.

Control of the structure of this transient complex may be accomplished with the aid of special catalysts of heterogeneous or homogeneous type (e.g., organoaluminium compounds with $TiCl_4$), proposed by Ziegler and Natta, which influence the geometry of the transient complex. Various factors aiding orientation of mono-

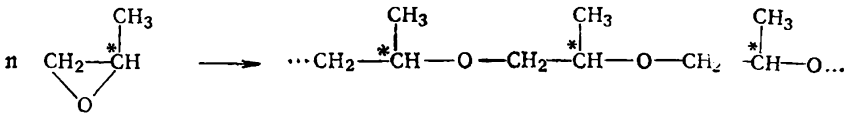
meric molecules immediately before their polymerization, may be utilized, such as the orienting effect of the crystal lattice of the monomer during its polymerization in the solid phase[1]. In some cases the temperature of the reaction may play a decisive part: as the addition of a new link with the same configuration as the preceding one yields more free energy than the addition of the next link with the inverse configuration, rather pure syndiotactic polymers may sometimes be obtained by using low temperatures (under 70°) during radical polymerization.

It should be pointed out, however, that in spite of the presence of asymmetric atoms, the majority of stereoregular polymers of the vinyl type are optically inactive. It is known that optical activity, which is due to the asymmetric carbon atom, depends on the substituents situated in the immediate neighbourhood of the atom. In a high-molecular-weight vinyl polymer the two neighbouring regions of the asymmetric carbon atom are identical. Only the carbon atoms of the end groups are fully asymmetrical, but their concentration in the total mass of the polymer is insignificant.

Because of this, synthesis of optically active polymers presents a separate problem.

The simplest logical approach to this problem is to use an optically active monomer.

For example, *L*-propylene oxide was polymerized with retention of configuration of the asymmetric carbon atom [103].



The first important conclusions concerning the polymerization of alkenes according to the radical mechanism were made by Pryanishnikov in 1928 [104]. When studying the polymerization of ethylene and pseudobutylene in a silent discharge, he noticed that this process resembles in general the polymerization of alkenes at high temperatures and pressures. Pryanishnikov came to the conclusion that polymerization involves not only rearrangement of hydrogen atoms but elimination and addition of hydrocarbon radicals as well.

Presently available data give a sufficiently detailed idea of the mechanism of radical polymerization of alkenes. The first stage of polymerization, initiated by the peroxide, is decomposition of

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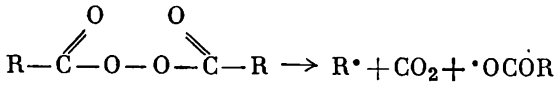
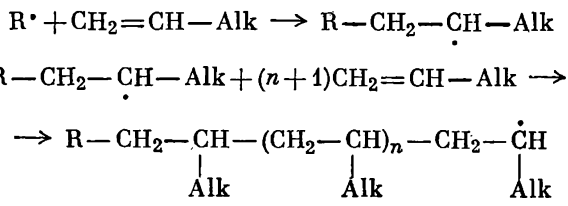
[1] Some interesting kinetic relationships of rapid polymerization in the solid phase have been shown in the work of Kargin and coworkers [99-102].

the latter to form free radicals.



If the reaction is initiated by oxygen, a peroxide or a free radical may form from the product of addition of oxygen to the alkene. In the case of thermal or photochemical polymerization a free radical may form as a result of rupture of a double bond or dissociation of a C — H bond.

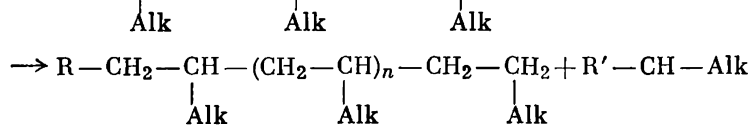
*Chain propagation.* A free radical R• reacts with an alkene as follows:



(a)

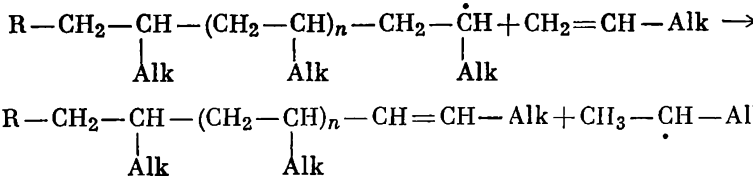
(b)

*Chain transfer.* A polymeric free radical may saturate itself by acquiring a hydrogen atom from a $R'—CH_2—Alk$ molecule (monomer, polymer or solvent):



(c)

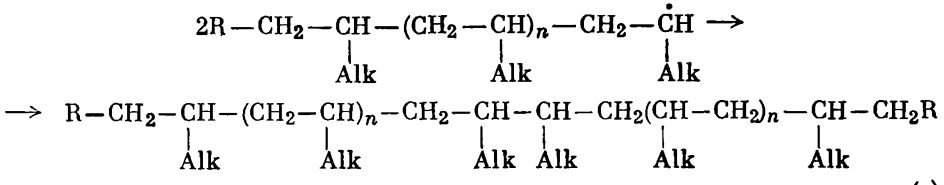
Chain transfer is also possible as a result of a hydrogen passing from a free radical of the polymer to a monomer molecule:



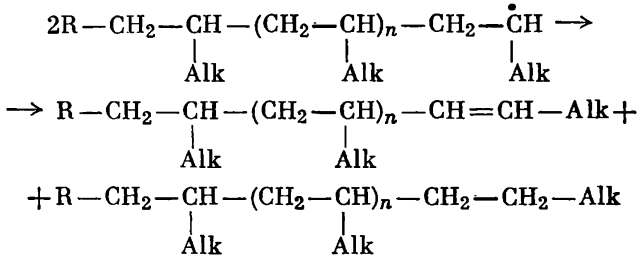
(d)

The free radicals R′ — CH — Alk and $CH_3$ — CH — Alk, formed in stages (*c*) and (*d*) start new chains as in stages (*a*) and (*b*).

*Chain termination.* Two free radicals (not necessarily the same) may recombine (*e*) or disproportionate (*f*).



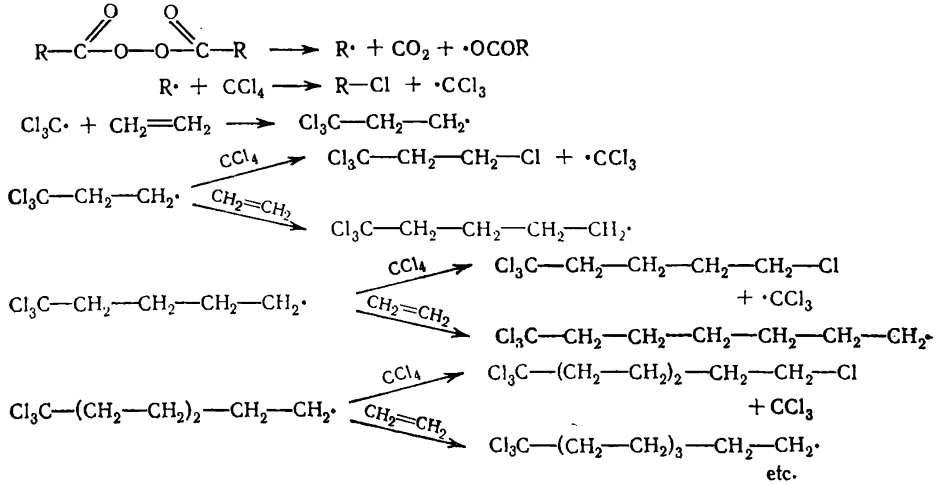
(e)



(f)

Chain termination may also occur as a result of the reaction of a polymer free radical with impurities contained in the monomer. It is therefore apparent that monomers of the highest purity should be used when polymers of very high molecular weight are desired*.

A unique reaction of radical polymerization is the polymerization of ethylene initiated by peroxides and terminated by carbon tetrachloride (telomerization):



Different telomerization products result predominantly depending on the conditions of the reaction. Telomerization is a convenient

* For review of radical polymerization see (105).

way of synthesizing ω-chloro monobasic fatty acids:

$$Cl-(CH_2-CH_2)_n-CCl_3 \xrightarrow{H_2O} Cl-(CH_2-CH_2)_n-C\begin{matrix}\nearrow O\\ \searrow OH\end{matrix}$$

It should be pointed out that telomerization in particular and polymerization under the action of radical reagents in general, may be accounted for only by reactions of kinetically independent free radicals. It is highly improbable that such processes could take place exclusively in a tangle of reactions (page 388) without forming free radicals as kinetically independent particles.

### 4-1.5 Alkylation of Alkanes by Alkenes

The reaction of alkylation of alkanes by alkenes discovered in 1932-35 is of great industrial importance, because it is used to synthesize branched hydrocarbons of high octane rating.

This alkylation may be thermal or catalytic. Propane and higher alkanes may be alkylated thermally. Such an alkylation requires high temperatures (about 500°) and pressures of 200-300 atm.

The reaction consists in addition of the alkane to the double bond of the alkene (hydrogen adds to one of the unsaturated carbon atoms and the alkyl radical to the other):

$$CH_3-CH_2-CH_3+CH_2=CH_2 \begin{matrix}\nearrow CH_3-CH_2-CH_2-CH_2-CH_3\\ \searrow CH_3\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH-CH_2-CH_3\end{matrix}$$

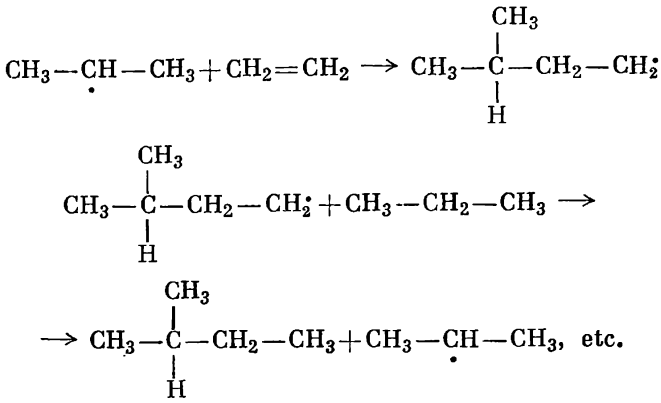
$$CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{C}}}}H+CH_2=CH_2 \begin{matrix}\nearrow CH_3\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH-CH_2-CH_2-CH_3\\ \searrow CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{C}}}}-CH_2-CH_3\end{matrix}$$

Thermal alkylation is evidently a free radical chain reaction the mechanism of which may be presented as follows:

$$CH_3-CH_2-CH_3- \begin{matrix}\xrightarrow{(a)} CH_3-\underset{\displaystyle \cdot}{\overset{\displaystyle \cdot}{C}}H-CH_3+\cdot H\\ \xrightarrow{(b)} CH_3-\underset{\displaystyle \cdot}{\overset{\displaystyle \cdot}{C}}H_2-CH_2\cdot+\cdot H\end{matrix}$$

Since secondary free radicals form more readily than primary ones, the main reaction products are derived from the isopropyl

radical:



*n*-Pentane forms in much smaller amounts than isopentane in this reaction.

As the tertiary hydrocarbon radical $(CH_3)_3C^{\cdot}$ forms more readily than the primary one $(CH_3)_2CHCH_2\cdot$, alkylation of isobutane by ethylene results in larger quantities of 2,2-dimethylbutane (yield 44%) than 2-methylpentane (11%).

Only alkanes containing tertiary hydrogen atoms are subjected to catalytic alkylation. The reaction proceeds under much milder conditions (temperature −30° to +100°, pressure 1-15 atm). Catalytic alkylation gives higher yields than thermal alkylation.

In catalytic alkylations acid catalysts are employed, which may be divided into two classes: (1) anhydrous Friedel-Crafts-Gustavson halide catalysts ($AlCl_3$, $AlBr_3$, $ZrCl_4$, $BF_3$; hydrogen halides are used as promoters for these catalysts) and (2) acids (concentrated sulphuric acid and liquid hydrogen fluoride). Thus, all of the catalysts used in alkylation are electrophilic reagents.

In all cases of catalytic alkylation of isoalkanes by alkenes not only condensation products of one isoalkane molecule with one or several alkene molecules are formed, but alkanes of intermediate molecular weight as well, i.e., a catalytic alkylation reaction is always accompanied by cracking. The compounds formed by catalytic alkylation are often of a different structure than those formed by thermal alkylation.

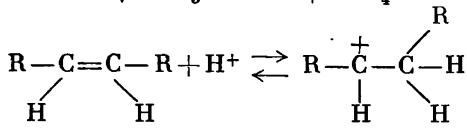
For instance, catalytic alkylation of isobutane by propylene results in: 2,3-dimethyl- and 2,4-dimethylpentane, 2,2,4-trimethyl- and 2,3,4-trimethylpentane, 2,3-dimethylbutane, 2-methylbutane. 2,2-Dimethylpentane which usually forms during thermal alkylation is not found in the products of catalytic alkylation.

The by-products of the catalytic alkylation of isobutane by isobutylene, which results predominantly in isooctane (2,2,4-tri-

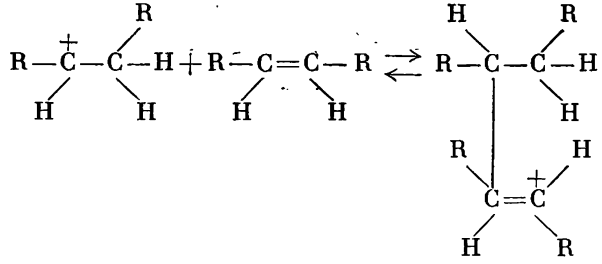
methylpentane), include: 2,3,3-trimethylpentane, 2,2,3-trimethylpentane, 2,3,4-trimethylpentane and 2,4-dimethylpentane.

The mechanism of catalytic alkylation of isoalkanes by alkenes is still largely unknown. However, in general terms it evidently takes the following course:

1. Addition of a proton to the alkene produces a carbonium ion:

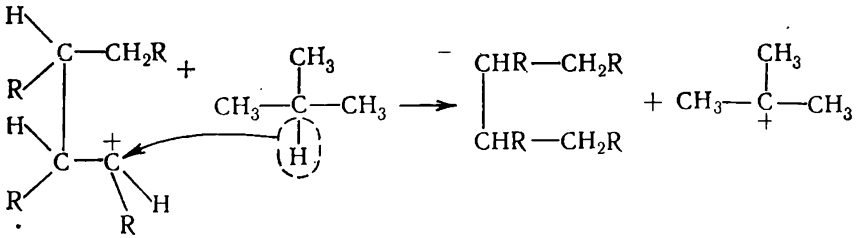


2. The resulting carbonium ion adds to a second alkene molecule to form a new carbonium ion:

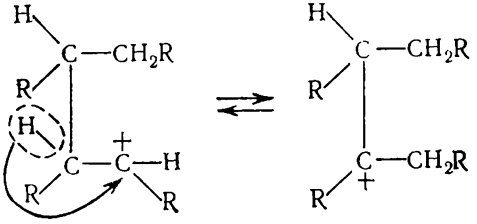


3. The carbonium ion formed in the second step may undergo one of the following transformations:

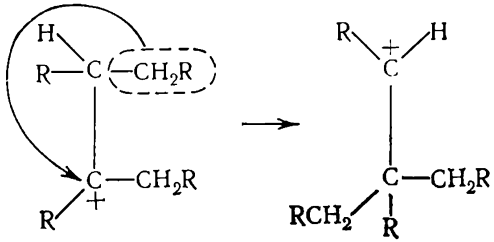
(a) It may remove an atom of hydrogen with an electron pair from the isoalkane molecule, e.g., from isobutane:



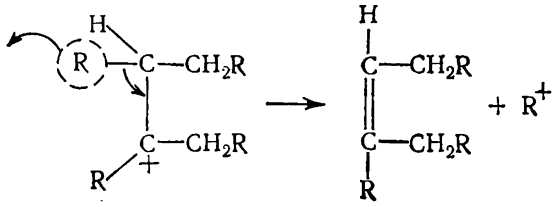
(b) A hydrogen atom with an electron pair may migrate from the α-carbon atom to the carbon atom carrying a positive charge:



(c) An alkyl group with an electron pair may migrate from the β-carbon atom to the newly formed carbonium ion:



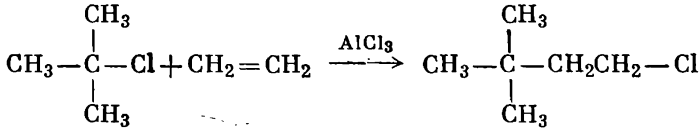
(d) And, finally, dissociation may occur with the formation of still another carbonium ion and an alkene:



There is indirect evidence that the individual steps of the complex reaction of catalytic alkylation of isoalkanes by alkenes are correct [106].

Step 1 can hardly arouse any doubt, because the ability of alkenes to add protons is generally known.

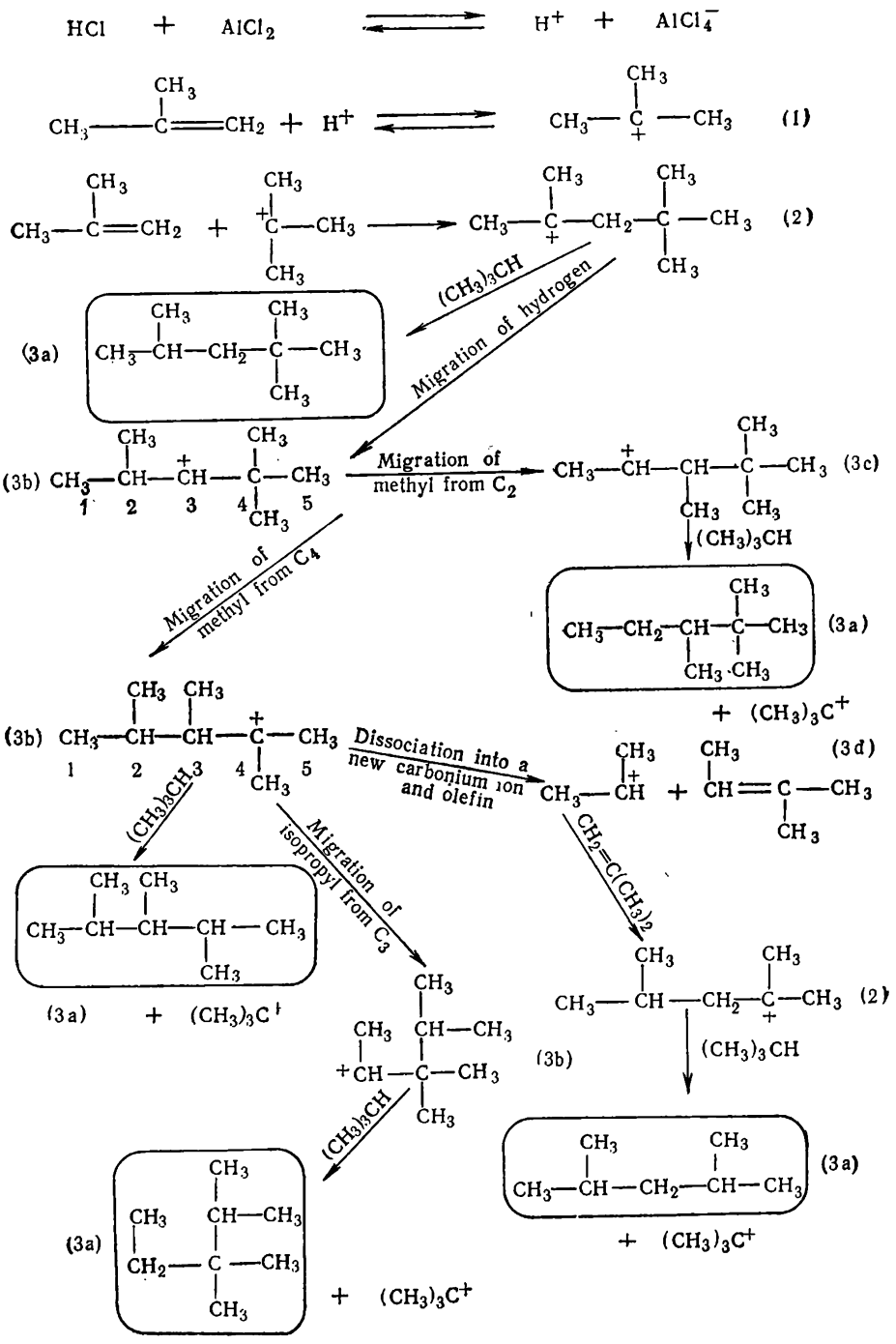
Step 2 is a case of the well-known addition of alkyl halides to alkenes in the presence of aluminium chloride, e.g.:



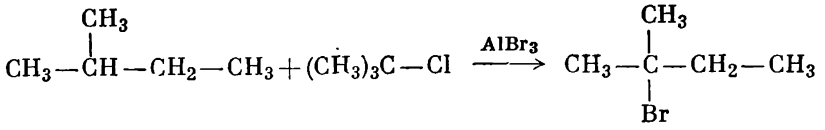
The role of aluminium chloride consists in abstracting a chloride anion from the alkyl halide and forming the carbonium ion:

Stages 3a, 3b, 3c, 3d are in agreement with the basic hypotheses of the theory of carbonium ions confirmed experimentally in a number of cases.

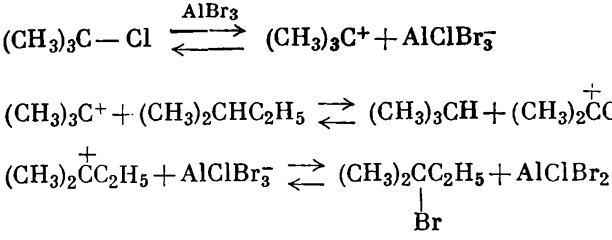
Thus, the probability of step 3a has been confirmed by a study of the reaction between isopentane and *tert*-butyl chloride in the presence of aluminium bromide.


HCl + AlCl2 ⇌ H+ + AlCl4−
(1)
(2)
(3a)
(3b)
(3c)
(3d)
(CH3)3CH
Migration of hydrogen
Migration of methyl from C2
Migration of methyl from C4
Dissociation into a new carbonium ion and olefin
CH2=C(CH3)2
Migration of isopropyl from C3
+ (CH3)3C+

*Tert*-amyl bromide forms rapidly at room temperature:



The latter may form only as a result of a sequence of reactions one of which is identical with step 3a:



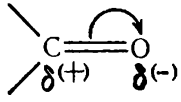
Using the mechanism just considered the results of alkylation of isobutane by isobutylene may be explained by the scheme shown on p. 307.

In conclusion it should be noted that the explanation given above for the role of aluminium chloride in the reactions involving alkyl halides, is simplified. Actually it has been proved that the acid $H^+AlCl_4^-$ cannot exist even for a short time. Besides, it is not clear from this explanation why the Friedel-Crafts reaction does not proceed in the absence of water.

Of considerable interest in connection with this is Nenitzescu's hypothesis, according to which the active catalyst is not aluminium chloride but a complex compound $AlCl_3 \cdot H_2O$, e.g., the acid $H^+[AlCl_3CH]^-$, which reacts with alkyl halides to form $Alk^+[AlCl_3OH]^-$. It is the latter compound and not $Alk^+[AlCl_4]^-$ that serves as the transfer agent for the alkyl cation.

## 4-2 ADDITION TO THE CARBON-OXYGEN DOUBLE BOND

Polarization of the π bond is characteristic of the carbonyl group. The π electrons are shifted towards oxygen which is the electrically more negative atom:



Therefore the carbonyl group has two centres: a positive (electrophilic, cationoid) on the carbon, and a negative (nucleophilic, anionoid) on the oxygen. In reactions of carbonyl compounds the deter-

minative role is that of the electrophilic centre at the carbon, because unlike alkenes, the carbonyl group easily adds nucleophilic reagents ($HCN$, $NH_3$, $NaHSO_3$).

All cations are electrophilic and all anions are nucleophilic reagents. Molecules generally have both nucleophilic and electrophilic reaction centres, however, in the vast majority of cases the reactivity of one of them is greater than that of the other. This circumstance is the criterion for deciding whether a molecule is an electrophilic or a nucleophilic reagent.

Consider the following series of reagents in heterolytic reactions:

$$Br_2, \quad HBr, \quad H_2O, \quad HCN$$

In heterolytic reactions the bromine molecule dissociates into a cation and an anion: $Br\left\{Br \rightarrow :\underset{\cdot\cdot}{\overset{\cdot\cdot}{Br}}^{(+)} + :\underset{\cdot\cdot}{\overset{\cdot\cdot}{Br}}:^{(-)}\right.$. Of these two ions the cation possesses greater energy and is therefore more reactive. This determines the nature of reactivity of the bromine molecules as a whole, and it is electrophilic. It is exactly the same in the case of reactions where free ions do not form but the bromine molecule undergoes heterolytic dissociation and reacts in a "reaction tangle".

In the hydrogen bromide molecule the difference in activity of the electrophilic and nucleophilic centres $\underset{\delta\oplus}{H}—\underset{\delta\ominus}{Br}$ is also rather clear-cut. The electrophilic centre (on the hydrogen) is much more active than the nucleophilic centre, as a result of which the hydrogen bromide molecule possesses electrophilic properties.

In the water molecule there is little difference between the activities of the electrophilic and nucleophilic centres $\underset{\delta\oplus}{H}—\underset{\delta\ominus}{OH}$. The activity of the electrophilic centre is not high; that is why water does not add to alkenes, for instance, in the absence of a catalyst. On the other hand, the activity of the nucleophilic centre is also low, because water, for example, does not add to aldehydes and ketones, with a few exceptions (page 313).

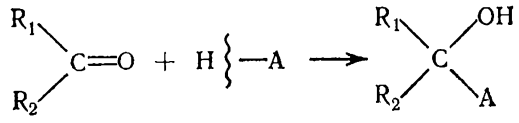
Finally, in the case of hydrocyanic acid $\underset{\delta\oplus}{H}—\underset{\delta\ominus}{CN}$ the reactivity of the molecule as a whole is determined by the nucleophilic centre, because the presence of a free electron pair on the carbon in the $C \equiv N^{(-)}$ ion makes its energy greater and reactivity higher than those of the $H^+$ ion. The anion $CN^{(-)}$ tends to attack the electrophilic centre of the reacting molecule and to share its electron pair with some other atom to form a covalent bond. This property of the $CN^-$ anion is responsible, in particular, for the low dissociation constant of HCN ($7 \times 10^{-10}$).

Thus, hydrocyanic acid is a nucleophilic reagent.

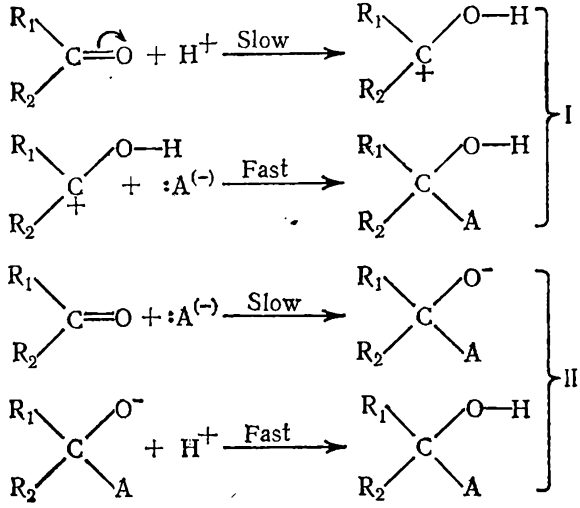
## 4-2.1 Mechanism of Addition of Nucleophilic Reagents

The causes of nucleophilic reactivity of carbonyl compounds can be cleared up by the following considerations.

By analogy with the addition reactions of alkenes, it may be suggested that addition to carbonyl groups is a two-stage process; thus for the reaction:



two mechanisms would seem possible:




Since reaction kinetics is determined by the slow step, the decision as to the true mechanism of addition to the carbonyl group rests on an evaluation of the rates of the slow stages of reaction mechanisms I and II.

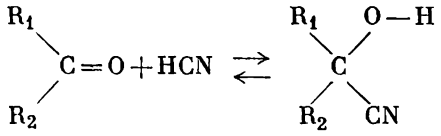
In the first case the slow stage of the reaction results in a cation with a positive charge on the carbon, in the second, in an anion with a negative charge on the oxygen.

The energy of the anion must be smaller than that of the cation. Numerous stable anions with a negative charge on the oxygen, such as $HO^-$, $AlkO^-$, etc., are known. On the other hand, cations with a positive charge on the carbon are very unstable, with the exception of cations of the triarylmethyl type.

Thus, the addition to carbonyl compounds must follow mechanism II, through the stage of stable ion formation.

Experimental facts confirm this theoretical reasoning.

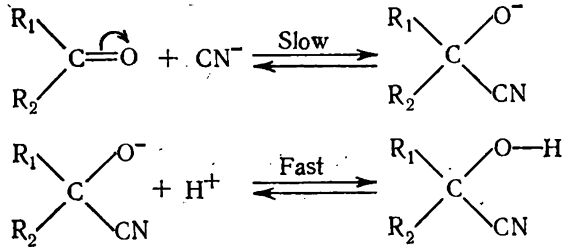
For instance, the cyanohydrin reaction,




which is a bimolecular reaction, is accelerated by the addition of bases or salts of weak acids, but not neutral salts, and is slowed down by the addition of acids [107]. It follows primarily from these facts that hydrocyanic acid does not add as a molecule. If the $H^+$ and $CN^-$ ions added simultaneously, the reaction would be termole-

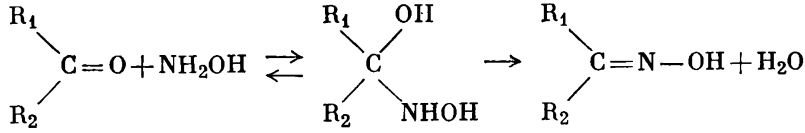
cular; its rate would depend on the concentration of the two ions and the addition of small quantities of acids or bases would not change it. Since increasing the $H^+$-ion concentration (addition of acids) decreases the rate of formation of cyanohydrin, $H^+$ ions apparently do not participate in the first, slow stage of the reaction. The $CN^-$ ions participate in this stage, because an increase in their concentration (addition of bases shifts the equilibrium $H-C\equiv N \rightleftarrows H^+ + CN^-$ to the right) accelerates the rate of formation of cyanohydrin.

Thus the mechanism of the cyanohydrin reaction is as follows*:




The addition to carbonyl compounds of organozinc and organomagnesium compounds, sodium bisulphite, etc., most probably follows the same mechanism as the addition of hydrocyanic acid.

The so-called substitution reaction of carbonyl compounds (with hydroxylamine, hydrazine, semicarbazide, etc.) undoubtedly passes through an addition stage:



The formation of addition products was proved by Hantzsch who isolated the addition product of hydroxylamine to chloral [119].

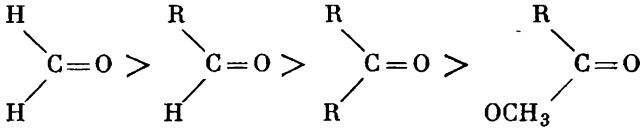
### 4-2.2 Effect of Groups Linked to the Carbonyl Group on Its Reactivity

The reactivity of the carbonyl group depends essentially on the nature of the groups linked with it. It is known that of all the carbonyl compounds the most reactive are aldehydes, and of the latter the most reactive is formaldehyde. The carbonyl group in ketones is less reactive. As to the carbonyl group in esters it bears little resemblance in properties to the carbonyl group of aldehydes and ketones.

---

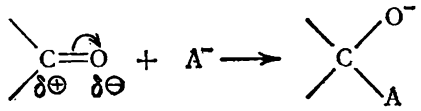
*The reaction is reversible. The equilibrium constants of a number of cyanohydrins have been determined [108].

The ability to add nucleophilic reagents is so low in this case that only the most energetic of them (e.g., organozinc and organomagnesium compounds) are able to add to esters:

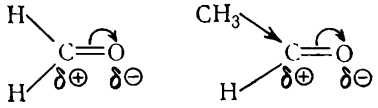


The reasons for the gradual decrease in reactivity of the carbonyl group in aldehydes, ketones and esters* compared to formaldehyde may be explained as follows.

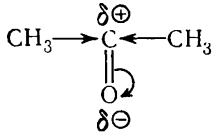
The first, slow stage of the addition reactions to the carbonyl group is an attack on the carbonyl carbon atom by the nucleophilic agent:



therefore, the reactivity of the carbonyl group must depend largely on the magnitude of the positive charge on the carbonyl carbon atom. The larger this positive charge, the more readily the addition of the nucleophilic reagent $A^-$, and therefore the reaction as a whole, will proceed. But as alkyl groups display a positive inductive effect, in this case, beginning with acetaldehyde, the positive charge of the carbonyl carbon in aldehydes must diminish compared to formaldehyde



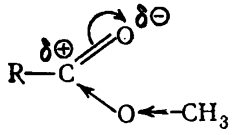
In ketones the carbonyl group is linked with two alkyl groups, the positive inductive effect of which lowers the positive charge of the carbonyl carbon even more than in aldehydes:



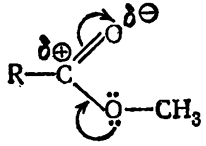
Finally, in esters the positive charge of the carbonyl group carbon atom is still smaller, being neutralized by the shift not only of the

* The comparison of electrophilic activity of acid derivatives is given on page 425.

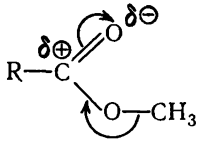
δ electrons of the O — $CH_3$ bond:



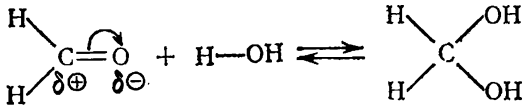
but of the *p* electrons of oxygen as well:



The net effect may be expressed as follows:

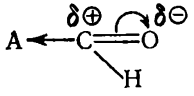


As distinct from higher aldehydes, formaldehyde, the carbonyl group of which is the most reactive toward nucleophilic reagents, apparently adds even such a weakly nucleophilic reagent as water:



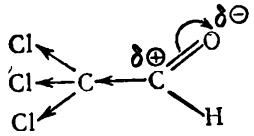
A study of the light diffusion spectra of aqueous formaldehyde shows that it contains only a minor amount of unhydrated $CH_2O$ molecules, because the spectra lack frequencies characteristic of the carbonyl group. However, the hydrated form of formaldehyde is unstable and cannot be isolated from solution.

If an atom of hydrogen in a formaldehyde molecule is replaced by any electron-attracting group, the positive charge of the carbon of the carbonyl group would naturally be expected to increase.

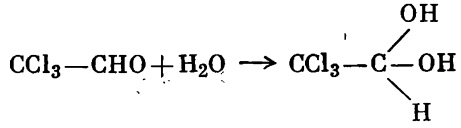


In such a case one would expect higher reactivity toward water and greater stability of the hydrates formed. Chloral possesses such

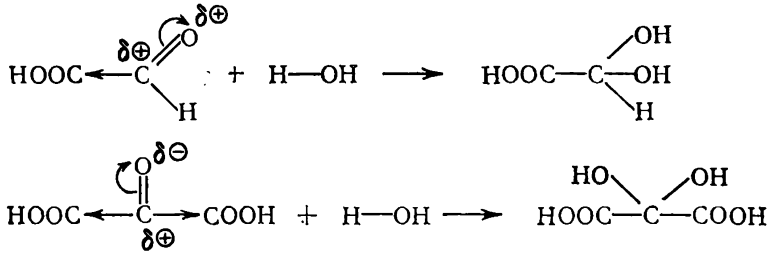
structural features:



The electron-attracting $CCl_3$ group increases the positive charge of the carbonyl carbon. Consequently chloral readily adds a molecule of water to form chloral hydrate:



The reasons for the formation of stable hydrates of glyoxylic and mesoxalic* acids are analogous:



In these cases the increase in the positive charge on the carbonyl group carbon is due to the shift of σ electrons from the carbonyl carbon to the carboxyl groups.

Petrenko-Kritchenko [110, 111] conducted extensive experimental research into the reactivity of the C = O group in various compounds.

The results of kinetic studies of the reactions of various ketones with hydroxylamine, phenylhydrazine and potassium bisulphite are given in Table 4-2 [110, 111].

From the data given in the table it is apparent that methyl ketones are the most reactive. Exchange of a methyl group for any other alkyl lowers the reactivity. This may be due to the greater inductive effect of higher alkyl groups, as well as to the increase in steric hindrance. Probably, both factors play a part. The greater

* The high reactivity of the carbonyl group of mesoxalic acid, exceeding that of the carbonyl group of aldehydes, shows that steric hindrance can play but a subordinate part in lowering the reactivity of the carbonyl group on passing from formaldehyde to normal higher aldehydes and then to ketones and esters (in the aliphatic series).

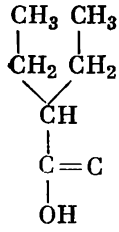
TABLE 4-2

**The Rates of Reaction of Ketones with Hydroxylamine, Phenylhydrazine and Potassium Bisulphite**

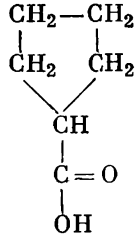
| Ketone or aldehyde | Rate in hours | | |
|---|---|---|---|
| | $NH_2OH$ | $C_6H_5NHNH_2$ | $KHSO_3$ |
| Acetone | 82 | — | — |
| Methylethyl ketone | 79.2 | — | — |
| Methylpropyl ketone | 74.6 | — | — |
| Methylhexyl ketone | 67.6 | — | — |
| Diethyl ketone | 37.9 | 11 | 1.8 |
| Ethylpropyl ketone | 36.8 | 10 | 2 |
| Dipropyl ketone | 31.4 | 7.5 | 0 |
| Methylisopropyl ketone | 33 | 15 | 2.7 |
| Ethylisopropyl ketone | 28.9 | — | — |
| Acetophenone | 9.2 | — | — |
| Benzaldehyde | 85 | — | — |
| Isobutyraldehyde | 76.7 | — | — |
| Cyclopentanone | 61.8 | 42.3 | 7 |
| Cyclohexanone | 92 | 39.7 | 35 |
| Cycloheptanone | 44.2 | 29.9 | 4.8 |
| Methyl cyclopropyl ketone | 9.1 | 5.6 | 0 |

reactivity of cyclic ketones (compare, for example, diethyl ketone and cyclopentanone) is probably due primarily to reduction of the steric hindrance owing to the definite orientation of the ring.

If, in this case, the determining influence were the inductive effect of the substituents, cyclic ketones would be less reactive, as it follows, for example, from a comparison of the strengths of diethylacetic and cyclopentanecarboxylic acids:



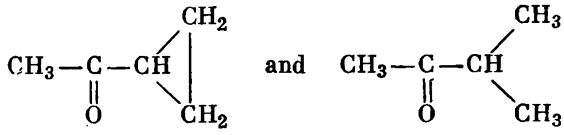
$K = 2.03 \times 10^{-5}$ at 25°



$K = 1.24 \times 10^{-5}$ at 24°

Since steric hindrance cannot affect the dissociation constants substantially, it is clear that the inductive effect of the tetramethylene group $CH_2—CH_2—CH_2—CH_2—$ is stronger than that of the two ethyl groups.

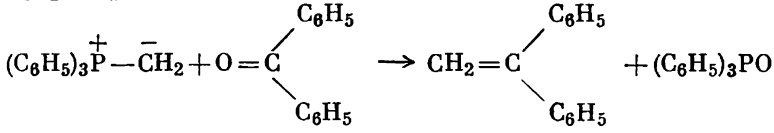
It is interesting that compounds having a three-membered ring are considerably less reactive than open-chain compounds:



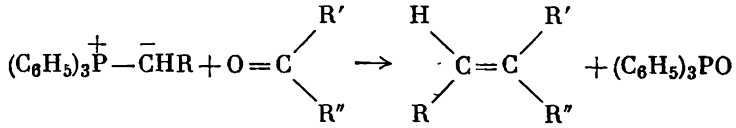
The three-membered ring resembles a double bond in a number of properties and here it has the same passivating influence on the carbonyl group as the double bond in methylvinyl ketone. The mechanism of this effect is not understood however.

### 4-2.3 Wittig Reactions*

In 1953 Wittig established [119] that methylenetriphenylphosphorane reacts with benzophenone to form 1,1-diphenylethylene and triphenylphosphine:

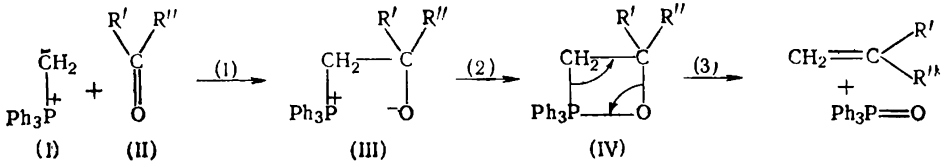


Later Wittig developed this reaction into a general method of converting the carbonyl group C=O to the C=C group:



This reaction became very important, for synthesis reactions, particularly in the chemistry of natural products.

A three-stage mechanism was proposed for this reaction [120]:



In the first stage alkylidenetriphenylphosphorane (I) reacts with the carbonyl compound (II) at the polarized carbonyl group resulting in a betaine (III) which is subsequently transformed into a four-membered compound (IV) with pentavalent phosphorus. The latter

* See [112-118] for reviews.

decomposes (on heating or spontaneously) into triphenylphosphine oxide and alkene.

The first stage proceeds the easiest when the carbonyl group is the most polarized and when the phosphorane is the most reactive. The occurrence of this stage is confirmed by the separation of a stable betaine (as a hydrobromide) in the reaction of methylenetriphenylphosphorane with benzaldehyde:

$$Ph_3\overset{+}{P}-\overset{-}{C}H_2 + PhCHO \longrightarrow Ph_3\overset{+}{P}-CH_2-\underset{|}{\overset{O^-}{C}}H-Ph \xrightarrow{HBr} \longrightarrow [Ph_3\overset{+}{P}-CH_2-CH(OH)Ph]Br^-$$

Of special significance, apparently, for the successful course of the reaction is stage (2)—the transformation of the betaine into a cyclic compound; if steric and electronic factors impede the formation of the cyclic compound, the reaction may terminate at the betaine stage.

The mechanism of the third stage is not clear, because the kinetics of Wittig's reaction has not yet been studied.

The stereochemistry of Wittig's reaction was studied by Shemyakin and coworkers [121] and by House and Rasmussen [122].

### 4-2.4 Stereochemistry of Addition Reactions at the Carbonyl Group

At present we do not have enough data to decide whether certain addition reactions at the carbonyl group are *cis*- or *trans*-additions; this is due to the fact that the conformation of the substance formed as a result of the reaction is lost immediately owing to free rotation of the C — O bond.

In the case of reactions of addition to the carbonyl group, however, there is another stereochemical problem which has been studied quite sufficiently.

However, if an asymmetric carbonyl compound, RCOR′ adds to the carbonyl group, a compound with an asymmetric carbon atom results:

$$RR'C=O + X-Y \longrightarrow RR'\overset{*}{C}\begin{matrix} OY \\ \diagup \\ \\ \diagdown \\ X \end{matrix}$$

If the initial carbonyl compound RCOR′ has no asymmetric carbon atom, a racemic mixture results from the addition reaction.

However, if the molecule RCOR′ contains an asymmetric carbon atom (especially in the alpha-position), a mixture of two diastereomers (*threo* and *erythro*) is formed, one of which will predominate.

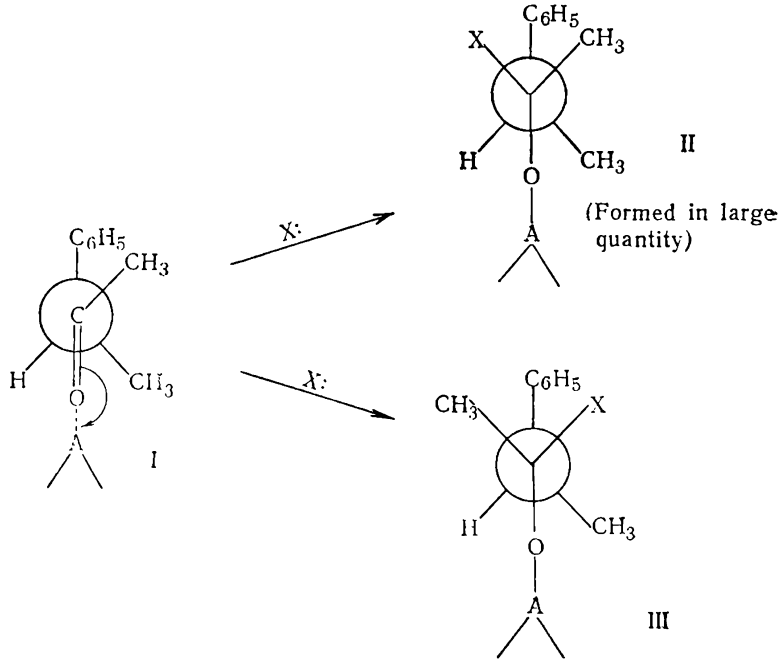
Usually the predominant stereoisomer is the one formed through the least sterically inhibited transition stage.

Consider, for example, the conversion of the ketone $C_6H_5CH(CH_3)-$ $-CO-CH_3$ into a carbinol either through a Grignard reaction or through reactions with hydride-ion donors [of the type $LiAlH_4$, $NaBH_4$ or $Al(iso\text{-}C_3H_7)_3$].

First of all it should be taken into account that in the course of these reactions the oxygen atom of the carbonyl group, apparently, participates in complex formation (with atoms of magnesium, aluminium and boron) prior to the attack on the carbonyl carbon by nucleophilic reagents.

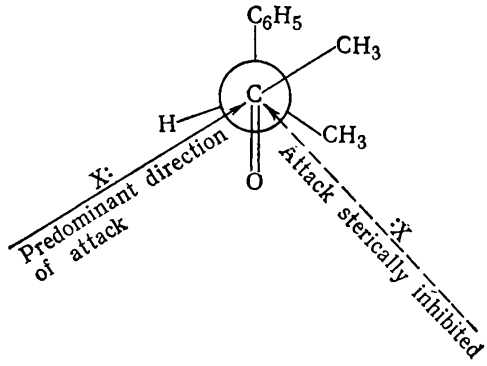
It should further be considered that the ketone molecule will predominantly be in conformation (1) in which the complex-linked carbonyl group (C = O . . . A) is furthest away from the bulky phenyl group.

The nucleophilic reagent (X:) must attack molecule (1) predominantly on the side where the small α-hydrogen atom is located, forming diastereomer II.

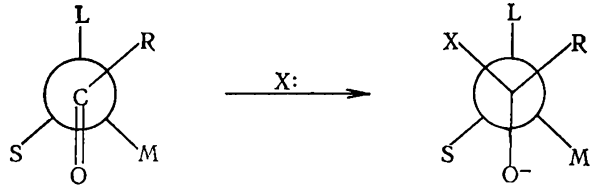



Attack on the side, where the bulkier methyl group is situated, is sterically inhibited, and therefore, diastereomer III is formed in smaller amounts.

The above reasoning as to "stereochemical control of asymmetric induction" (*Cram's rule*) is applicable in many analogical cases. According to Cram's rule, if an asymmetric centre forms during an addition reaction adjacent to one already present in the molecule, the double bond in the more preferred transition state will be blocked by two less voluminous α-substituents and the attacking reagent will approach the double bond on the less sterically inhibited side [123].




According to Cram's rule the course of the reaction may be represented schematically in the following manner (the large substituent is designated L, the small one S, the medium one M).




This rule does not apply to addition reactions under the conditions of heterogeneous catalysis, because in those cases the stereochemistry is determined by the orientation of the molecules adsorbed on the catalyst surface.*

### 4-2.5 Addition of Nucleophilic Reagents in the Presence of Catalysts

The catalytic addition of molecules to carbonyl compounds and nitriles may be differentiated from noncatalytic additions of the type of cyanohydrin reactions.

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* For a discussion of more complex questions of the stereochemistry of addition reactions to the carbonyl group in the alicyclic series see [114].

Aldol condensation proceeding under the influence of basic substances may serve as a typical example of catalytic addition to the carbonyl group:

$$R-CH_2-CHO + R-CH_2-CHO \longrightarrow R-CH_2-CH(OH)-\underset{\displaystyle R}{\underset{|}{CH}}-CHO$$

The function of the catalyst (usually NaOH or KOH) consists in removal of the α-hydrogen atom from the aldehyde molecule in the form of a proton; the resulting organic anion adds to the carbonyl group of a second molecule forming a new carbon-carbon bond. The mechanism of the reaction may be represented by the following scheme:

$$R-CH_2-CHO + \overset{(-)}{OH} \underset{}{\overset{\text{Slow}}{\rightleftharpoons}} R-\overset{(-)}{\underset{\cdot\cdot}{CH}}-CHO + H_2O \qquad \text{(I)}$$

$$R-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}\underset{\displaystyle H}{\diagdown} + :\overset{(-)}{\underset{\displaystyle R}{CH}}-CHO \xrightarrow{\text{Fast}} R-CH_2-\overset{\displaystyle (-)}{\underset{\displaystyle H}{\overset{\displaystyle :\ddot{O}:}{C}}}-\underset{\displaystyle R}{\underset{|}{CH}}-CHO \qquad \text{(II)}$$

$$R-CH_2-\overset{\displaystyle (-)}{\underset{\displaystyle H}{\overset{\displaystyle :\ddot{O}:}{C}}}-\underset{\displaystyle R}{\underset{|}{CH}}-CHO + HOH \rightleftharpoons R-CH_2-\overset{\displaystyle OH}{\underset{\displaystyle H}{\overset{|}{C}}}-\underset{\displaystyle R}{\underset{|}{CH}}-CHO + OH^{(-)} \qquad \text{(III)}$$

Of the two stages I and II the former is the slower one, because kinetic investigations have shown [125] that aldol condensation is a first-order reaction with respect to the aldehyde.

The ratio of the slow stage I to the fast stage II varies depending on the structure of the reacting carbonyl compound. Thus, in the case of acetaldehyde the rate of stage II is so great that stage I is practically irreversible. This was proved experimentally by carrying out aldol condensation in deuterium oxide. If stage I were reversible, deuterium would link with the α-carbon atom:

$$:\overset{(-)}{CH_2}-CHO + D_2O \rightleftharpoons CH_2D-CHO + \overset{(-)}{OD} \rightleftharpoons :\overset{(-)}{CHD}-CHO + HOD, \text{ etc.}$$

Actually, no deuterium exchange occurred [126]. This confirms that stage II must follow stage I at once, making the latter practically irreversible. Unlike acetaldehyde, aldol condensation of acetone, carried out in deuterium oxide, yields diacetone alcohol containing deuterium [127], i.e., the difference between the rates of stages I and II is smaller in the case of aldol condensation of acetone than in the case of acetaldehyde.

The products of aldol condensation lose water readily to form α,β-unsaturated carbonyl compounds.

Undoubtedly, aldol condensation is the first stage of a whole series of well-known condensations of carbonyl compounds. Among these are condensations of aldehydes with aldehydes or ketones in the presence of alkali [128], condensation of aldehydes or ketones with malonic, acetoacetic or cyanoacetic esters or nitro compounds in the presence of organic bases [129], and the Perkin reaction consisting in the condensation of aldehydes with acid anhydrides in the presence of a carboxylic acid salt [130].

All these reactions may be expressed by a single general equation:

$$R{-}CHO + CH_2R'R'' \longrightarrow R{-}CH{=}CR'R'' + H_2O$$

(R′ and R″ being groups with electron-acceptor properties).

The Claisen acetoacetic condensation [131] resembles the above reactions:

$$R{-}\overset{\overset{O}{\parallel}}{C}{-}OAlk + CH'R''COX \longrightarrow R{-}CO{-}CR'R''{-}COX + HOAlk$$

(COX = COOAlk and COAlk)

A very important theoretical question is the role of catalysts in condensations of this type.

Catalysts of a basic nature may act on the aldehyde component or on the component having a reactive methylene group. The first point of view is shared by many discoverers of condensation reactions (Knövenagel, Claisen). Thus, Knövenagel [132] held that in the condensation of aldehydes with malonic, acetoacetic and cyanoacetic esters the organic base first adds to the aldehyde group. This point of view arose as a result of isolation of compounds of the type:

$$RCH(OH)NHR',\ RCH(NHR')_2 \text{ and } RCH(NR'R'')_2$$

It was postulated that substances of this type react easily with compounds containing a reactive methylene group, for example:

$$R{-}CH(OH)NHR' + CH_2\begin{matrix}\diagup\ COOC_2H_5\\ \diagdown\ COOC_2H_5\end{matrix} \longrightarrow R{-}CH(OH){-}CH\begin{matrix}\diagup\ COOC_2H_5\\ \diagdown\ COOC_2H_5\end{matrix} + R'NH_2$$

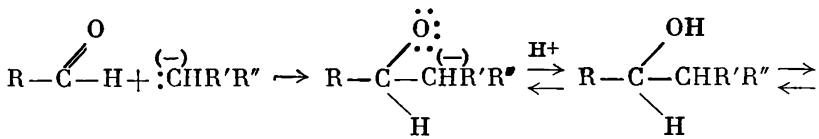
$$R{-}CH(OH){-}CH(COOC_2H_5)_2 \longrightarrow R{-}CH{=}C(COOC_2H_5)_2 + H_2O$$

However, this postulate failed to explain why tertiary bases catalyze such condensations. Besides, the fact of isolation of the

addition products of aldehydes and amines is no proof that they are intermediates in this reaction.

According to current concepts [133] the role of basic catalysts consists in the removal of the α-hydrogen atom from the molecule containing the active methylene group. The organic anion formed adds to the carbonyl compound, forming an aldol anion. The latter adds a proton yielding aldol, which readily undergoes irreversible dehydration.

$$B + CH_2R'R'' \rightleftarrows BH^+ + \overset{(-)}{:}CHR'R''$$

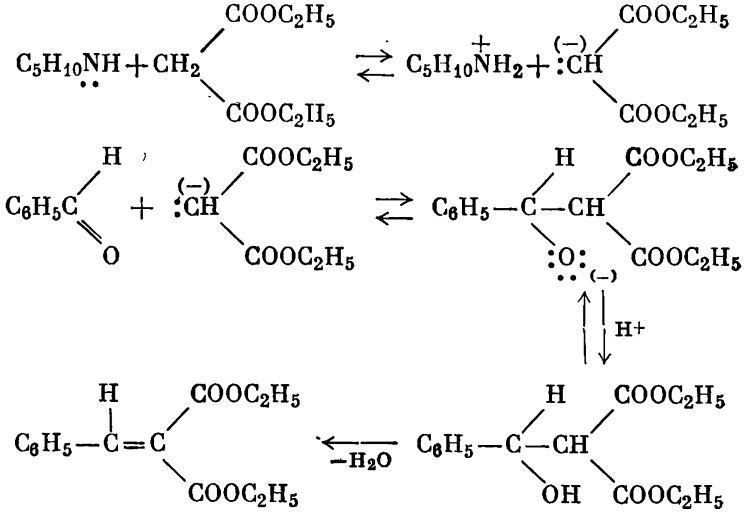


$$\rightleftarrows R-CH=CR'R'' + H_2O$$

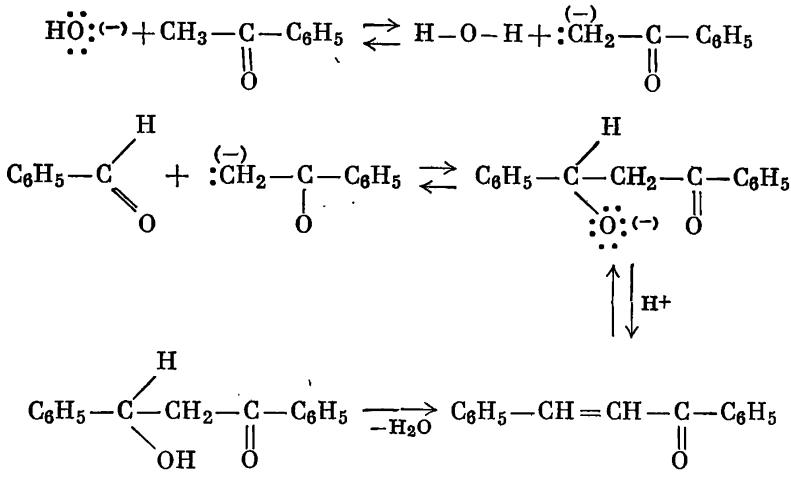
($B$ is a base: $OAlk^{(-)}$, $OH^{(-)}$, $CH_3COO^{(-)}$, $R_3N$:, etc.)

In conformity with these general concepts of the role of the basic catalyst, the mechanisms of various catalytic reactions of addition to the carbonyl group should be as follows:

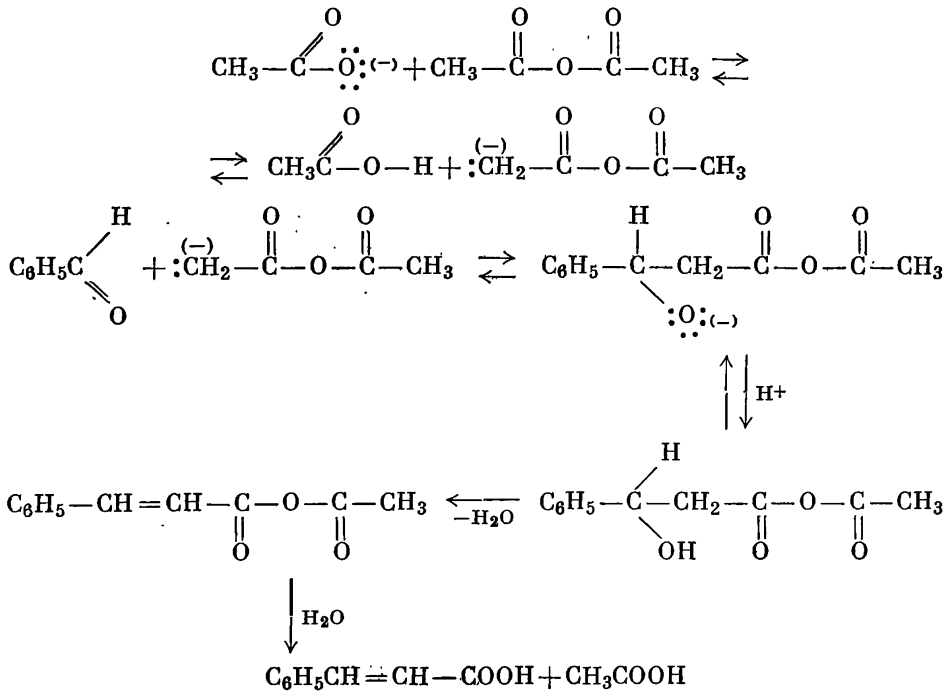
*Reaction of benzaldehyde with malonic ester in the presence of piperidine (Knövenagel's reaction)*



*Reaction of benzaldehyde with acetophenone in the presence of caustic soda (Claisen's reaction)*



*Reaction of benzaldehyde with acetic anhydride in the presence of sodium acetate (Perkin's reaction)*



For several decades opinions of chemists on the part played by acetic anhydride and sodium acetate were contradictory. Perkin believed that cinnamic acids form as a result of the condensation of aldehyde with the acid anhydride, and that the sodium salt acts as a catalyst. Wittig, on the contrary, basing his opinion on the formation of α-ethylcinnamic acid when a mixture of benzaldehyde, acetic anhydride and sodium butyrate were heated to 100°, thought that the acid salt condensed with benzaldehyde and the anhydride acted as a catalyst. Wittig's views were widely accepted for a long time. They are still not infrequently given in some modern textbooks on organic chemistry.

In his investigations, however, Wittig did not take into consideration that acetic anhydride reacts readily with salts of higher acids when heated, for example:

$$2C_3H_7COONa + (CH_3CO)_2O \underset{\longleftarrow}{\overset{100°}{\longrightarrow}} 2CH_3COONa + (C_3H_7CO)_2O$$

The equilibrium is displaced pronouncedly toward the higher acid anhydride; it was the latter that under the conditions of the experiment gave α-alkylcinnamic acid.

That under the usual conditions of Perkin's reaction it is specifically the aldehyde and not the salt of the acid that reacts with the aldehyde is proved by other facts. Thus, benzaldehyde condenses readily with acetic anhydride in the presence of organic and inorganic substances of a basic nature (potassium carbonate, triethyl amine and others), but does not condense with sodium acetate in the presence of the same catalysts or dehydrating substances.

This does not mean that under more drastic conditions salts of fatty acids cannot react with aldehydes directly. For example, by raising the reaction temperature from 180° to 240° *o*-chlorocinnamic acid can be obtained from *o*-chlorobenzaldehyde and potassium acetate.

Under these conditions the first stage of the reaction apparently consists in the reaction between two molecules of the salt:

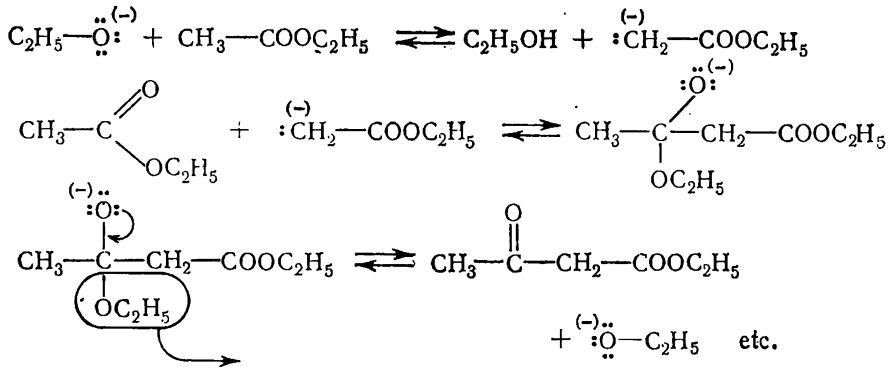
$$CH_3—COO^- + CH_3—COO^- \longrightarrow CH_3—COOH + {}^-CH_2—COO^-$$

The resulting anion $^-CH_2 — COO^-$ then reacts with the aldehyde.

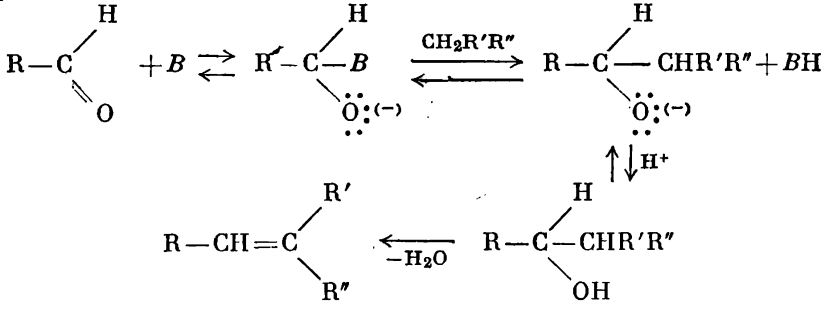
Lead acetate, which possesses much more reactive α-hydrogen atoms (page 150), can condense with benzaldehyde under ordinary conditions to form cinnamic acid with a good yield [134]:

$$2C_6H_5—CHO + (CH_3COO)_2Pb \longrightarrow (C_6H_5—CH=CH—COO)_2Pb + 2H_2O$$

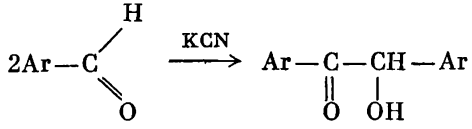
*Acetoacetic condensation (Claisen condensation)* [135]



Despite the high probability of the above reaction mechanisms of catalytic addition to the carbonyl group it must be kept in mind that they are of a hypothetical nature. There is no definite experimental proof that removal of a proton from the second component is the only (or even the main) function of the catalysts. It is probable that a more important function of the catalyst is activation of the carbonyl groups of the aldehydes or esters. In the light of this hypothesis the general mechanism of the above condensations could be pictured as follows:



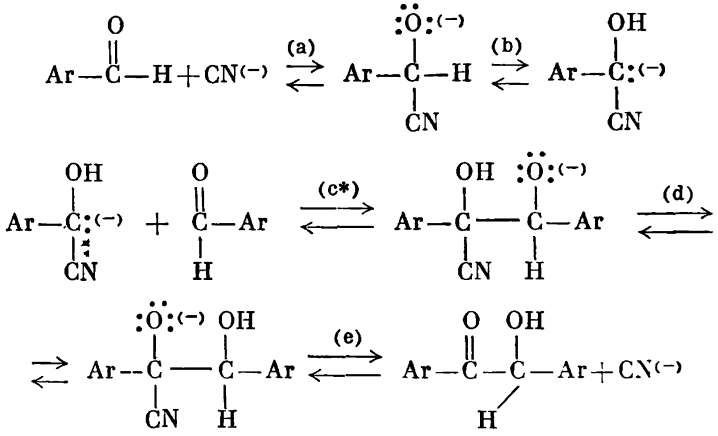
There is no doubt that in some cases the catalyst acts as an activator of the carbonyl group. This is so, for instance, in the benzoin condensation. The *benzoin condensation* [136] consists in the condensation of two molecules of an aromatic aldehyde in the presence of sodium or potassium cyanides:



The reaction rate obeys the equation $v = k\ [\mathrm{ArCHO}]^2\ [\mathrm{CN}^-]$. The reaction is reversible, is not accelerated by the addition of

HCN or alkali and does not take place at all if there are strong directing groups of the first or second type in the *o*- or *p*-position of the aromatic ring of the aldehyde.

All these peculiarities of the benzoin condensation can be accounted for, by assuming the following mechanism:



Since benzoin condensation is a third-order reaction, the slowest step determining the rate of the process as a whole must be stage (c) or stage (d). It is more probably stage (c), in which the new carbon-carbon bond is formed.

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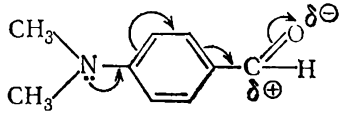
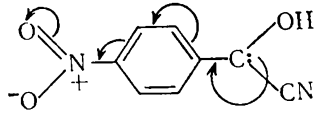
* The presence of strong directing groups of both the first and the second type in the *o*- or *p*-position of an aromatic aldehyde should prevent stage (*c*).

In the case of a strong directing group of type 1, for example:



the aldehyde group is inactivated with regard to nucleophilic reagents owing to the decrease in the positive charge on the carbonyl carbon.

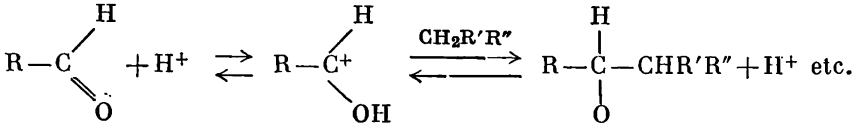
On the other hand, in the presence of a strong directing group of the second type, for instance:



the anion, formed by the addition of $CN^-$ to the aldehyde, may possess insufficiently strong nucleophilic properties owing to the electron pair being drawn away by the nitro group. This may result in inability of such an anion to add to the carbonyl group of another aldehyde molecule.

Benzoin condensation will not occur in either extreme case.

It is known that aldol condensation may take place under the influence of acid catalysts too. In this case the role of the catalyst consists apparently in activating the aldehyde carbonyl group:

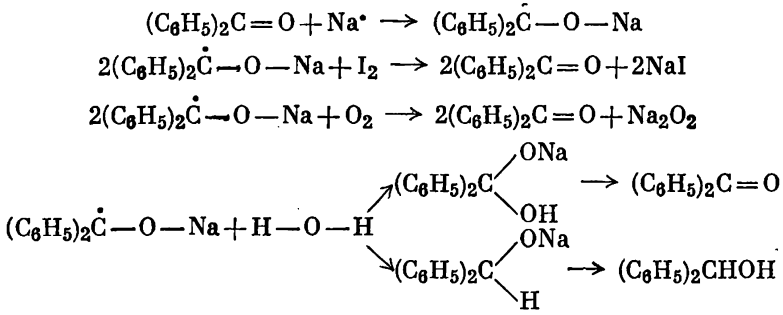


The organic cation formed as a result of the addition of proton to the aldehyde, reacts with the second component. The usual reaction of electrophilic substitution takes place at the saturated carbon (linked with mobile α-hydrogen atoms), resulting in a new carbon-carbon bond and freeing a proton capable of continuing the chain reaction.

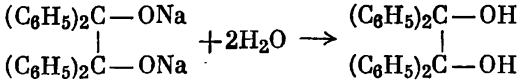
## 4-2.6 Radical Addition to the Carbonyl Group

It was discovered in 1891 [137], that when metallic sodium is dissolved in air-free solutions of aromatic ketones in dry ether, substances of a dark blue colour result.

Schlenk and Weickel [138] came to the conclusion that these materials, called ketyls, contain a trivalent carbon, because they react rapidly with iodine and oxygen, like triphenylmethyl, regenerating the original ketone and not the dimeric product. When decomposed by water they produce a mixture of the initial ketone and the corresponding alcohol



rather than pinacone, which should have formed if ketyls were compounds of tetravalent carbon:



The structure of metal ketyls as free radicals rather than pinacones is also confirmed by the following reactions:

$$(C_6H_5)_2\dot{C}-O-Na + CH_3I \longrightarrow (C_6H_5)_2C\begin{matrix}\diagup ONa \\ \diagdown CH_3\end{matrix} \xrightarrow{H_2O} (C_6H_5)_2C\begin{matrix}\diagup OH \\ \diagdown CH_3\end{matrix}$$

$$(C_6H_5)_2\dot{C}-O-Na + (C_6H_5)_3C-Cl \longrightarrow (C_6H_5)_2C=O + (C_6H_5)_3C^{\bullet} + NaCl$$

By analogy with the reaction between triphenylmethyl and metallic sodium, metal ketyls react slowly with an excess of sodium, yielding violet disodium derivatives:

$$(C_6H_5)_2\dot{C}-O-Na + Na\cdot \longrightarrow (C_6H_5)_2C\begin{matrix}-O \\ | \\ Na\end{matrix}\quad\begin{matrix}| \\ Na\end{matrix}$$

The latter can also be formed by the action of sodamide on the corresponding alcohols in liquid ammonia:

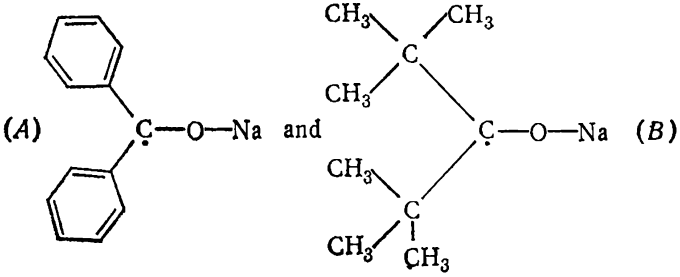
$$(C_6H_5)_2CH-OH + 2NaNH_2 \longrightarrow (C_6H_5)_2C\begin{matrix}-O \\ | \\ Na\end{matrix}\quad\begin{matrix}| \\ Na\end{matrix} + 2NH_3$$

Solutions of the metal ketyls in dioxane are paramagnetic. This is an indisputable physical proof of their free-radical character. At the same time magnetic measurements have shown that aromatic ketyls exist in a reversible equilibrium with diamagnetic pinacolates:

$$\begin{matrix}Ar_2C-O-Na \\ | \\ Ar_2C-O-Na\end{matrix} \rightleftarrows 2Ar\dot{C}-O-Na$$

Aliphatic ketyls prepared by Favorsky and Nazarov [139] from di-tertiary ketones, as, for example, from di-*tert*-butyl ketone, rapidly undergo complete dimerization.

Such a difference in the behaviour of aromatic and aliphatic ketyls

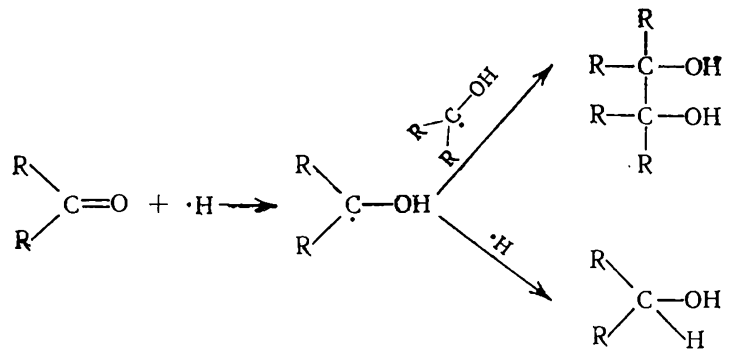



is quite understandable because the former, (A), are structurally close to free radicals of the triphenyl type, and the latter, (B), actu-

ally should resemble the simplest free alkyl radicals because of the presence of a localized electron on their carbon atom (see Chapter 5).

In many cases, electrolytic reduction of carbonyl compounds probably also consists in homolytic addition to the carbonyl group.

Electrolytic reduction of ketones results in pinacones; under similar conditions aldehydes yield glycols. These products form evidently as a result of dimerization of intermediate neutral radicals (A):



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# 5

# FREE RADICALS

## 5-1 BRIEF HISTORICAL REVIEW

The term "radical" was introduced into chemistry by Guyton de Morvaux and Lavoisier; the latter included in this concept simple radicals (elements), as well as complex radicals, pointing out that inorganic radicals are usually elements, while organic radicals consist at least of carbon and hydrogen, and often contain phosphorus and nitrogen.

In 1815 Gay-Lussac prepared cyanogen, which, in his opinion, was the first radical isolated in the free state.

From that time on and approximately up to the middle of the 19th century works on radicals aroused a lively interest among chemists.

Liebig, Woehler, and Laurent worked on the benzoyl radical, Bunsen on cacodyl, Frankland on methyl, and Kolbe on ethyl radicals.

As the majority of chemists of that period did not recognize Avogadro's law, they could not be sure they were dealing with the radicals, say, methyl, ethyl, benzoyl or with ethane, butane and benzil.

The gradual recognition of Avogadro's law and determination of the molecular weight of the assumed radicals soon showed that actually not a single free radical had been isolated because the molecular weight of these imaginary radicals was twice their theoretical weight.

From 1860 to 1890 the theory of tetravalency of carbon (which excluded the possibility of the existence of free radicals) became generally accepted.

Thus, an important proposition of the theory of chemical structure, the idea of tetravalent carbon, arose and was confirmed largely owing to the numerous unsuccessful attempts to isolate free radicals, that is, groups of atoms containing a carbon with a valence of less than four. It is natural, under the circumstances, that Gomberg's announcement [1] in 1900 of the preparation of the free triphenylmethyl radical was greeted by chemists with disbelief.

However, experiments carried out irreproachably by Gomberg himself, and the works of a number of investigators, among them Chichibabin, Markovnikov, Kermann, Fluersheim and Schmiedlin, confirmed that the first free radical had been obtained. Gomberg's discovery gave birth to the chemistry of free radicals which developed very rapidly. Besides triphenylmethyl, a whole series of free radicals of the triphenylmethyl series were prepared and their properties were investigated; biradicals were synthesized.

Aromatic ketyls were studied and found to be free radicals. Favorsky and Nazarov obtained and investigated aliphatic metal ketyls.

It was shown that the ability to form free radicals is not limited to the carbon atom. Radicals of mono-, di-, and tetravalent nitrogen and of monovalent oxygen were discovered.

All the radicals mentioned can exist indefinitely if certain precautions are taken.

The question of the theoretical possibility of existence of the simplest radicals such as methyl and ethyl remained unsolved for almost three decades after Gomberg's synthesis of triphenylmethyl, until in 1929 Paneth obtained methyl and ethyl radicals by thermal decomposition of tetramethyl and tetraethyl lead respectively.

If the study of free radicals during the first three decades of this century was of theoretical interest only, the subsequent study of short-lived free radicals unexpectedly clarified the nature of chemical processes of great practical importance (polymerization and pyrogenic processes, autoxidation and others).

## 5-2 TRIARYLMETHYL RADICALS

When triphenylmethyl bromide reacts with a metal, say, silver, one would expect hexaphenylethane to form:

$$2(C_6H_5)_3CBr + 2Ag \longrightarrow (C_6H_5)_3C-C(C_6H_5)_3 + 2AgBr$$

One would expect this to be a stable compound of low reactivity. However, Gomberg succeeded in obtaining it only on complete exclusion of air. Hexaphenylethane is a colourless crystalline substance. When dissolved in ether yellow solutions result. Hexaphenylethane solutions react instantaneously with the air oxygen, iodine, nitrogen oxide and other reagents yielding derivatives of triphenylmethyl.

All these properties, quite unusual for hydrocarbons, suggested the hypothesis that hexaphenylethane dissociates into free triphenylmethyl radicals in solution:

$$(C_6H_5)_3C-C(C_6H_5)_3 \rightleftarrows 2(C_6H_5)_3C\cdot$$

The latter react with $O_2$, $I_2$, NO, etc.:

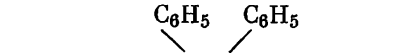
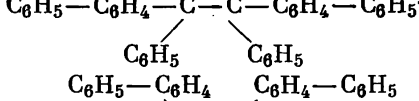
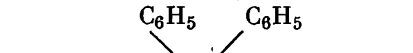
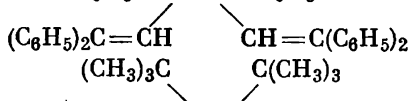
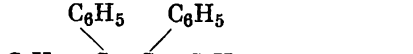
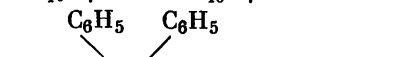
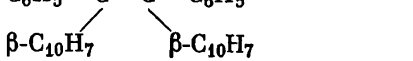
$$2(C_6H_5)_3C\cdot + O_2 \longrightarrow (C_6H_5)_3C-O-O-C(C_6H_5)_3$$
$$2(C_6H_5)_3C\cdot + I_2 \longrightarrow 2(C_6H_5)_3C-I$$
$$(C_6H_5)_3C\cdot + NO \longrightarrow (C_6H_5)_3C-NO$$

The hypothesis of dissociation of hexaphenylethane and other hexaarylethanes into triarylmethyl radicals was confirmed by determination of molecular weights, on the basis of which the degree of dissociation was calculated. The apparent molecular weights of hexaarylethanes can be determined by the cryoscopic method with but a low degree of accuracy (error up to 10%); however, this method is quite suitable for qualitative comparisons of the degrees of dissociation of these compounds.

Table 5-1 shows that the degree of dissociation of hydrocarbons $R_3C-CR_3$ into radicals $R_3C\cdot$ increases with increasing number of aromatic rings.

TABLE 5-1

**Dissociation of $R_3C-CR_3$ Compounds**

| $R_3C-CR_3$ Compounds | Percentage dissociation in $C_6H_6$ at 5° (concentration 2-3%) |
|---|---|
| $(CH_3)_3C-C(CH_3)_3$ | 0 |
| $(C_6H_5)_3C-C(C_6H_5)_3$ | 2-3 |
|  | 15 |
|  | 79 |
| $(C_6H_5-C_6H_4)_3C-C(C_6H_4-C_6H_5)_3$ | 100 |
| $(C_6H_5)_3C-(C_6H_5)_2C-C(C_6H_5)_2-C(C_6H_5)_3$ | 100 |
| $(O_2N-C_6H_4)_3C-C(C_6H_4-NO_2)_3$ | 100 |
|  | 80 |
|  | 74 |
|  | 60 |
|  | 33 |
|  | 24 |

* All the substituents are in *para*-positions.

The degree of dissociation of hexaphenylethane into triphenylmethyl can be also determined colorimetrically, because the hydrocarbon is colourless while the radical is yellow.

Table 5-2 lists the dissociation constants and heats of dissociation of hexaphenylethane in different solvents.

Despite the considerable differences in dissociation constants, the heat of dissociation of hexaphenylethane has apparently the same value in all solvents, $11.3 \pm 1$ kcal/mole.

TABLE 5-2

**Dissociation Constants and Heats of Dissociation of Hexaphenylethane in Different Solvents [2]**

| Solvent | Dissociation constant $K \times 10^4$ at 20° | Heat of dissociation, kcal |
|---|---|---|
| Propionitrile . . . . . | 1.2 | 11.1 |
| Ethyl benzoate . . . . | 1.67 | 12.0 |
| Acetophenone . . . . . | 1.70 | 11.50 |
| Dioxane . . . . . | 2.5 | 11.6 |
| Bromobenzene . . . . . | 3.7 | 11.5 |
| Ethylene bromide . . . | 3.9 | 11.4 |
| Benzene . . . . . | 4.1 | 11.3 |
| Chloroform . . . . . | 6.9 | 10.5 |
| Carbon disulphide . . . | 19.2 | 11.0 |

A dependable method of determining the degree of dissociation of hexaarylethanes is by measuring the magnetic susceptibility of their solutions.

TABLE 5-3

**Dissociation Constants and Heats of Dissociation of Hexaphenylethane in Decimolar Benzene Solution Obtained by Magnetic Susceptibility Measurements**

| Temperature °C | 100 α* | Dissociation constant $K$ | Heat of dissociation |
|---|---|---|---|
| 23 | 2.4 | $1.5 \times 10^{-4}$ | $11.6 \pm 1.7$ kcal |
| 75 | 8.9 | $53 \times 10^{-4}$ | |

* The Greek letter α is the degree of dissociation.

Besides enabling reliable differentiation between dissociation into radicals and dissociation into ions*, this method can also be used for determining the degree of dissociation of highly coloured materials.

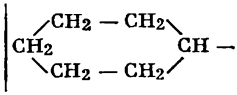
* Free radicals are always paramagnetic.

The degrees of dissociation of hexaphenylethane in decimolar benzene solution are given in Table 5-3.

Degrees of dissociation of para-substituted hexaarylethanes determined by this method are shown in Table 5-4.

TABLE 5-4

**Dissociation of $(p\text{-}RC_6H_4)_3C - C(C_6H_4R\text{-}p)$ Compounds in Decimolar Benzene Solution at 29°**

| R | $C_2H_5$ | $n\text{-}C_3H_7-$ | $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH-$ | $(CH_3)_3C-$ | $\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>\!CH-$ |  |
|---|---|---|---|---|---|---|
| $100\cdot\alpha$ | 17 | 21 | 26 | 27 | 33 | 22 |

It should, however, be pointed out that the magnetic susceptibility measurements which were used for determining the dissociation of substituted ethanes are erroneous due to the fact that the diamagnetism of the free radical itself could not be measured or estimated with certainty [3, 4]. Therefore, the figures given in Tables 5-3 and 5-4 may have errors as large as $\pm 50\%$.

This makes the method of electronic spin resonance (ESR) extremely important. As the phenomenon of paramagnetic resonance is applicable to electrons of paramagnetic substances only, the ESR method provides a way of determining directly the presence of unpaired electrons, making it unnecessary to consider the diamagnetism of the undissociated substance.

Free radicals can also be determined by taking advantage of their property of catalyzing *ortho-para*-transitions of hydrogen.

Hydrogen molecules exist in the *ortho-* and *para*-states, the difference being that in *ortho*-hydrogen the nuclear spins of the atoms are symmetrical and in *para*-hydrogens unsymmetrical. *Ortho-* and *para*-hydrogens have a small but noticeable difference in physical properties. The composition of an equilibrium mixture of *ortho-* and *para*-hydrogens depends on the temperature. Thus, the content of *para*-hydrogen in the mixture at 20° K is 99.82%, but at room temperature or above it reaches a minimum value of 25%.

Conversion of *para*-hydrogen into *ortho*-hydrogen and vice versa under ordinary conditions and in the absence of catalysts is a very slow process. However certain substances strongly catalyze the conversion even at very low temperatures. Among them are charcoal and nickel.

Of great interest is the conversion of hydrogen under the conditions of a homogeneous system, because it has been calculated [5] that equilibrium should be achieved rapidly under the influence of the magnetic field of paramagnetic molecules. Experiments

have confirmed this assumption. Thus, rapid conversion takes place in the gas phase in the presence of such paramagnetic molecules as oxygen, nitrogen oxide and nitrogen dioxide.

Naturally, the conversion of *para*-hydrogen into *ortho*-hydrogen was utilized for the determination of free organic radicals, such as triphenylmethyl [6] and more complex ones [7]. Solid organic radicals, like diphenylpicrylhydrazyl [8], also catalyze the conversion of *para*-hydrogen.

Though the *para*-hydrogen conversion method of determination of radicals is a simple one, it has been used very seldom in the past 20 years.

This is due, evidently, to two reasons: (1) the mathematical expression for calculating the effectiveness of conversion of *para*-hydrogen into *ortho*-hydrogen under the influence of radicals is very complicated, and (2) the sensitivity of the method is limited by the fact that slow conversion of *para*- into *ortho*-hydrogen takes place even in diamagnetic solutions as a result of the reaction of hydrogen with the atoms of the solvent (with hydrogens, in particular), which possess nuclear spins causing slight paramagnetism.

The most convenient methods for preparing triarylmethyl radicals are those of Gomberg and the Arbuzovs.

According to the former a metal (most often zinc, copper or mercury) is reacted with a solution of triarylchloromethane in an organic solvent (ether, benzene, carbon disulphide, ethyl acetate):

$$n\mathrm{Ar_3CCl} + \mathrm{Me} \longrightarrow n\mathrm{Ar_3C\cdot} + \mathrm{MeCl}_n$$

The Arbuzovs method [9] consists in reducing triarylbromomethane with sodium diethylphosphate:

$$\mathrm{Ar_3C{-}Br} + \mathrm{Na{-}P(=O)(OC_2H_5){-}OC_2H_5} \longrightarrow \mathrm{Ar_3C\cdot} + \mathrm{NaBr} + \mathrm{PO(OC_2H_5)_2}$$

Free triarylmethyl radicals can also be obtained by the reduction of triarylhalomethanes or triarylcarbinols in strongly acidic solution with the aid of vanadium dichloride, titanium trichloride and chromium dichloride [10].

## 5-2.1 Causes of Formation and Stability of Free Triarylmethyl Radicals

The classical theoretical concepts of organic chemistry were unable to explain the formation and existence of free radicals such as triphenylmethyl. Nor could the existence and the properties of the latter be accounted for by classical electronic concepts.

Solution of these problems became possible only when the quantum-mechanical properties of electrons were taken into consideration.

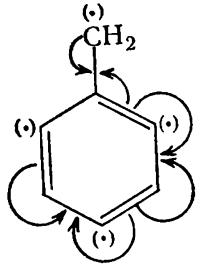
It is known that a large amount of energy is required to cause homolytic rupture of the carbon-carbon bond. For example, to split an ethane molecule into two methyl radicals requires 84.2 kcal/mole

$$CH_3{:}CH_3 \longrightarrow 2CH_3\cdot$$

However, the energy of such a carbon-carbon bond rupture may be lower if aromatic groups are linked with the carbon atoms (the bond between which is to be broken). Thus, to rupture the C — C bond in symmetrical diphenylethane only 68 kcal/mole is required.

$$C_6H_5{-}CH_2{:}CH_2{-}C_6H_5 \longrightarrow 2C_6H_5{-}CH_2\cdot$$

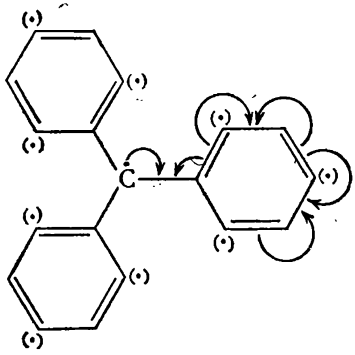
Such a marked decrease of the energy of rupture in diphenylethane as compared with ethane is due to the fact that the benzyl radical possesses less energy than the methyl radical. This energy decrease may be understood by considering the probability of conjugation of the odd electron of the methylene group with the $\pi$ electrons of the benzene ring:




As a result of this the electron cloud of the valence electron is not localized on the methylene group carbon, but is actually spread over four carbon atoms. This is the reason for the lower energy, because higher energy is peculiar to groups in which the valence electron is localized on a single carbon atom (such as methyl or ethyl).

If both methylene hydrogen atoms in the benzyl group are replaced by phenyl groups the valence electron of the resulting triphenylmethyl radical is still more delocalized, and consequently, its free energy is still lower, because the valence electron in triphenylmethyl may interact with the $\pi$ electrons of all three benzene rings

(as shown below for only one ring; each arrow indicates a shift of one electron):

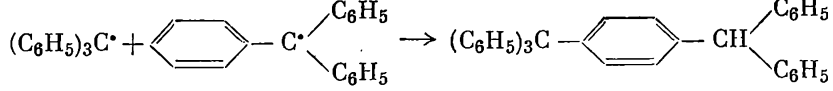


Naturally, the energy of the C — C bond rupture causing the formation of triphenylmethyl radicals must be even lower than that of the rupture of the bond in diphenylethane. Indeed, only 11-12 kcal/mole are required to rupture the C — C bond in hexaphenylethane. Such a low dissociation energy causes hexaphenylethane to dissociate readily into triphenylmethyl radicals.

The high probability of interaction of the valence electron of triphenylmethyl with the $\pi$ electrons of benzene rings (delocalization of the electron cloud) is the reason why in reactivity triphenylmethyl does not resemble such radicals as methyl or ethyl, where the valence electron is localized on a single carbon atom. While radicals like methyl and ethyl, capable of existing for a very short time only, react vigorously with a large number of different substances including even the noble metals, radicals such as triphenylmethyl are rather inert chemically, and react readily only with the most active reagents (oxygen, halogens, nitrogen oxide, etc.).

From the above discussion it follows that in triphenylmethyl a definite "radical activity" should be exhibited by the *ortho-* and particularly (because of the absence of steric hindrance) by the *para*-carbon atoms of the benzene rings.

The formation of *p*-benzhydryltetraphenylmethane from triphenylmethyl radicals may serve as experimental confirmation of the above hypothesis.

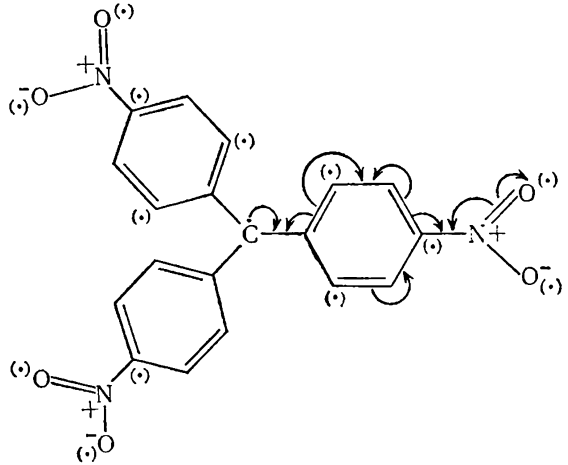


In this reaction triphenylmethyl reacts with a radical reagent (triphenylmethyl) specifically on the *para*-carbon atom.

The stability of triarylmethyl radicals is due largely to the nature of the aryl groups. In general, the stability of free radicals increases

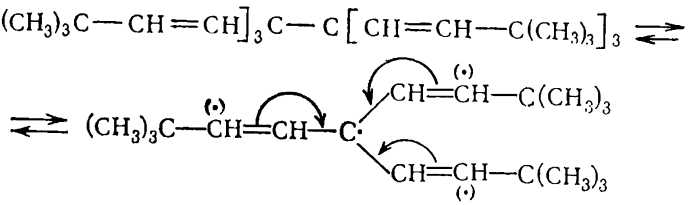
with increasing probability of delocalization of the electron cloud of the valence electron. For example, hexaphenylethane dissociates in benzene (concentration 2-3%) at 5° to an extent of 2-3%, while under the same conditions hexa-*p*-biphenylethane and decaphenylbutane are 100% dissociated into tri-*p*-phenylmethyl and pentaphenylethyl radicals respectively (Table 5-1).

Hexa-*p*-nitrophenylethane is 100% dissociated, because the presence of the nitro group (see pages 479, 484) considerably increases the probability of delocalization of the cloud of the odd electron of the free radical:



Steric factors and the weight of the radicals are mostly of secondary importance for the dissociation of hexaarylethanes. This is evident, for example, from a comparison of the degrees of dissociation of hexa-β-naphthylethane and hexa-*p*-nitrophenylethane. The former is only 24% dissociated, while the latter dissociated to the extent of 100% even in the solid state.

The dissociation of hexa-(*tert*-butylvinyl)ethane points in the same direction:



Steric factors undoubtedly have a definite influence on the ease of formation and properties of triarylmethyl radicals. Even the simplest of them, triphenylmethyl, possesses a "propeller-like" rather than planar structure.

Steric factors are particularly important in cases where hexaarylethanes have substituents in *ortho*-positions.

The influence of steric factors is evident from the degrees of dissociation of substituted hexaphenylethanes listed in Table 5-5.

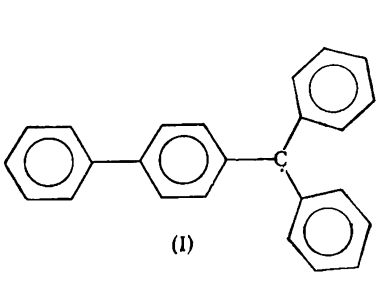
TABLE 5-5

**Degree of Dissociation of Substituted Hexaphenylethanes (in Decimolar Benzene Solution, Determined by Magnetic Susceptibility Measurements) [11]**

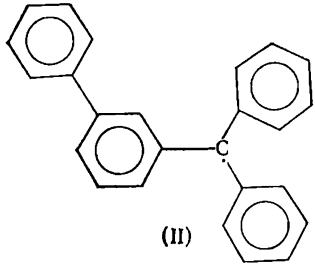
| Substance | Percentage dissociation $100 \cdot \alpha$ |
|---|---|
| $[p\text{-}CH_3C_6H_4(C_6H_5)_2C-]_2$ | 5 |
| $[p\text{-}(CH_3)_2CH-C_6H_4(C_6H_5)_2C-]_2$ | 8-10 |
| $[o\text{-}CH_3C_6H_4(C_6H_5)_2C-]_2$ | 25 |
| $[o\text{-}C_2H_5C_6H_4(C_6H_5)_2C-]_2$ | 33 |
| $[p\text{-}C_6H_5-C_6H_4(C_6H_5)_2C-]_2$ | 12 |
| $[m\text{-}C_6H_5-C_6H_4(C_6H_5)_2C-]_2$ | 13 |
| $[\alpha\text{-}C_{10}H_7(C_6H_5)_2C-]_2$ | 54 |
| $[(o\text{-}C_2H_5C_6H_4)_2C_6H_5C-]_2$ | 82 |
| $[(p\text{-}C_6H_5-C_6H_4)_2C_6H_5C-]_2$ | 18 |

Table 5-5 shows that two methyl groups in the *ortho*-position influence the degree of dissociation more than four extra benzene rings in *para*-positions.

The behaviour of di-*m*-biphenyltetraphenylethane and di-*p*-biphenyltetraphenylethane illustrates the relative effect of steric and electronic factors. If the electronic factors were the determining factors, the latter compound would be the more dissociated one, because the probability of delocalization of the electron cloud of the unpaired electron in the free radical formed (I) is greater than in radical (II):



(I)

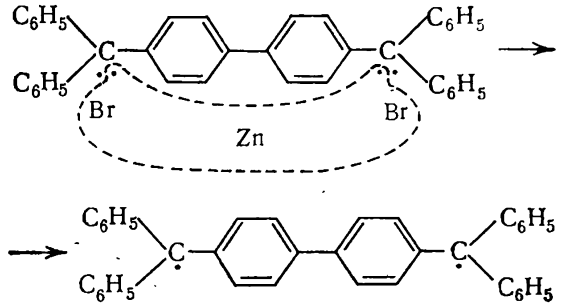


(II)

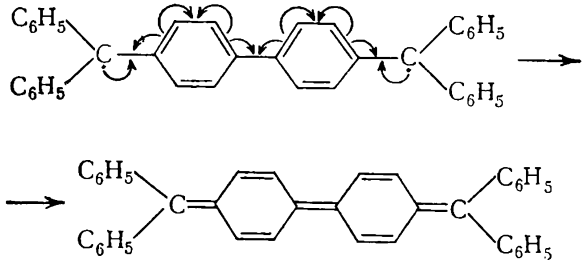
However, actually [12] both ethane derivatives dissociate in benzene solution at 25° to approximately the same extent: 11-14%.

Thus, in the general case the ease of formation and properties of triarylmethyl radicals depend not only on their electronic structure but on steric factors, as well.

Biradicals exhibit a number of interesting properties. The action of zinc on *p*, *p'*-dibenzhydrylbiphenyl dibromide would be expected to result in the formation of the corresponding paramagnetic biradical.

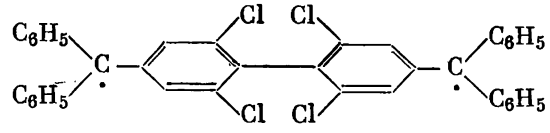



In reality, however, the result is Chichibabin's hydrocarbon, which is practically devoid of paramagnetic properties [13]. This is due to the fact that the electron clouds of the two unpaired electrons and the $\pi$ electrons, the axes of which may lie parallel (or nearly so) interact in such a way that the valence electrons also participate in the formation of the bonds:



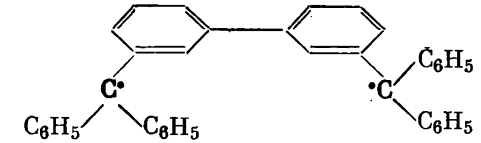

It should be pointed out that Chichibabin's hydrocarbon catalyzes *ortho-para*-interconversion of hydrogen [14]. This anomaly became understood after Chichibabin's hydrocarbon was studied by the spin resonance method [15], the accuracy of which is much higher as compared with conventional magnetic susceptibility measurements. It was found that 4-5% of the hydrocarbon is in biradical form.

Pairing of the odd electrons becomes impossible if the coplanarity of the benzene rings is disturbed. Thus, in the tetrachloro derivative of Chichibabin's hydrocarbon



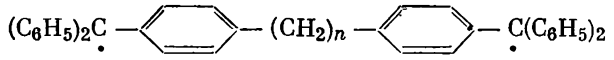
the chlorine atoms prevent planar configuration of the molecule, as a result of which the above compound is a true paramagnetic biradical.

Schlenk's hydrocarbon is capable of existence for another reason.



There is nothing in this biradical to prevent planar molecular configuration, but the two valence electrons do not interact because the *meta*-substituents do not influence each other noticeably. This peculiarity of conjugated systems was pointed out earlier (page 58).

Biradicals of the following general formula are also capable of existence:



In this case the triphenylmethyl systems are separated by a chain of saturated carbon atoms, through which no interaction of unpaired electrons can take place.

## 5-3 FREE RADICALS WITH NITROGEN AND OXYGEN

Stable radicals of elements other than carbon are also known. Such, for instance, are organic radicals of nitrogen and oxygen. In all such radicals the atom carrying the valence electron is linked with aromatic nuclei, as a result of which the explanation given for the formation and properties of triarylmethyl radicals is applicable to stable radicals of other elements too.

Some examples of nitrogen radicals are radicals of diaryl nitrogen, hydrazyl radicals and diphenyl nitrogen oxide.

Tetraphenylhydrazine resembles hexaphenylethane in a number of properties. It is a colourless crystalline solid, stable in storage. However, when its solutions are heated it dissociates forming green diphenyl nitrogen radicals [16]:

$$(C_6H_5)_2N{-}N(C_6H_5)_2 \rightleftarrows 2(C_6H_5)_2N\cdot$$

Diphenylnitrogen, like triphenylmethyl, reacts with nitrogen oxide very fast:

$$(C_6H_5)_2N\cdot + \cdot NO \longrightarrow (C_6H_5)_2N{-}NO$$

The radical character of diphenylnitrogen is confirmed by its reaction with triphenylmethyl, as a result of which a tertiary amine is formed:

$$(C_6H_5)N\cdot + \cdot C(C_6H_5)_3 \longrightarrow (C_6H_5)_2N{-}C(C_6H_5)_3$$

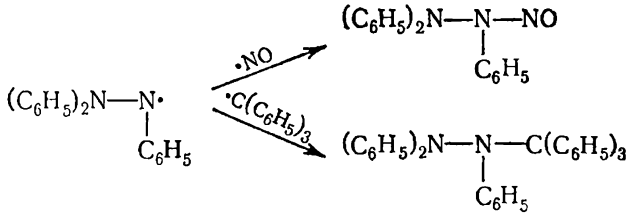
Unlike triphenylmethyl, diphenylnitrogen reacts neither with oxygen nor with iodine. This is apparently due to the fact that such reactions are endothermic and result in the formation of unstable products.

The tendency of the N — N bond to dissociate is most strikingly expressed in the tetrazane series [17], obtained by the oxidation of triarylhydrazines:

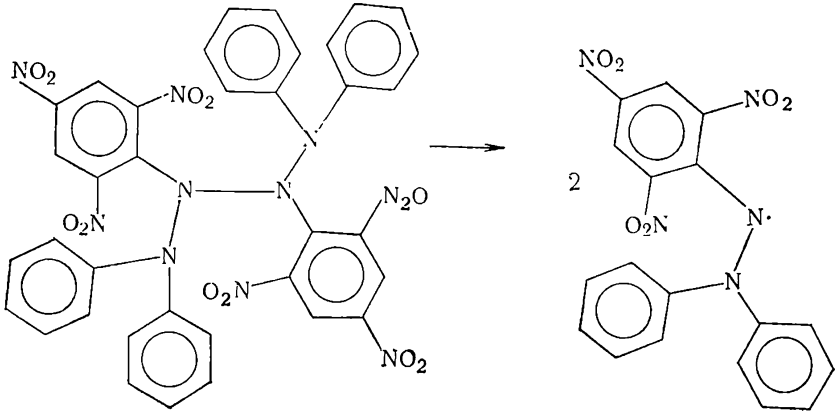
$$(C_6H_5)_2N-\underset{\displaystyle C_6H_5}{\underset{|}{N}}-H \xrightarrow[\text{ether}]{PbO_2} \underset{\text{Hexaphenyltetrazane (light green)}}{(C_6H_5)_2N-\underset{\displaystyle C_6H_5}{\underset{|}{N}}-\underset{\displaystyle C_6H_5}{\underset{|}{N}}-N(C_6H_5)_2} \rightleftarrows \underset{\text{Triphenylhydrazyl (dark blue)}}{2(C_6H_5)_2N-\dot{\underset{\displaystyle C_6H_5}{\underset{|}{N}}}}$$

The dissociation of hexaphenyltetrazane is perceptible even at room temperature.

Triphenylhydrazyl reacts immediately with nitrogen oxide and slowly with triphenylmethyl:



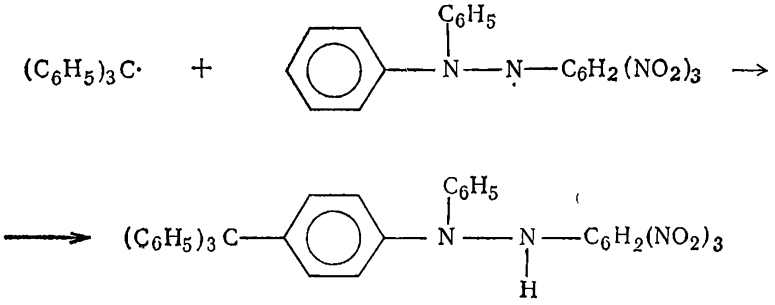

Dipicryltetraphenyltetrazane dissociates completely into 2,2-diphenyl-1-picrylhydrazyl radicals:



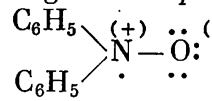

Such easy dissociation is favoured both by steric factors and by the probability of delocalization of the electron cloud in the radical formed.

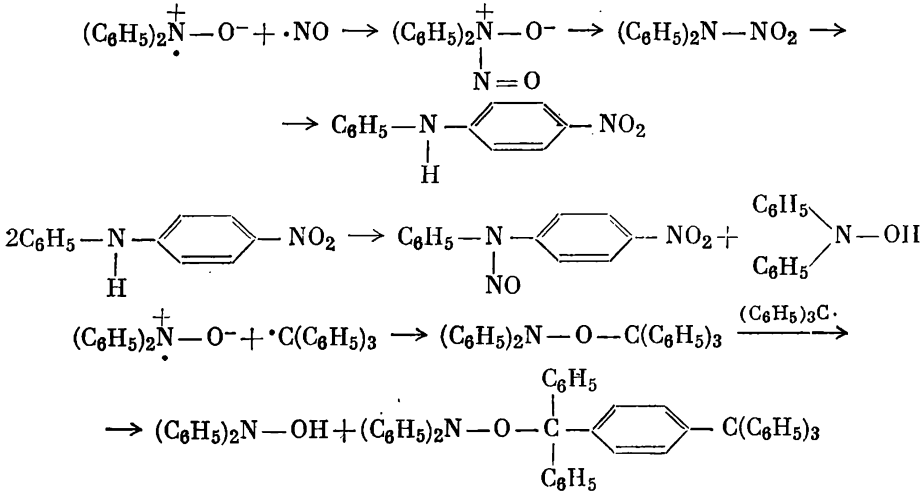
The existence of diphenylpicrylhydrazine has been proved cryoscopically, by magnetic susceptibility measurements [18] and by the electronic spin resonance spectra [19]. Currently diphenylpicrylhydrazyl is often utilized as a standard for determining the magnetic properties of radicals [15].

The chemistry of diphenylpicrylhydrazyl has been studied insufficiently [20]. The structure of the reaction product with triphenylmethyl has been established:



Triphenylmethyl does not form a bond with the nitrogen, but reacts with the benzene ring in the *para*-position.

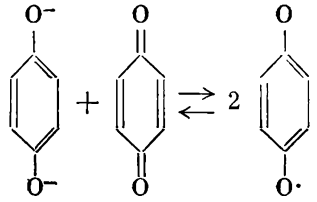
Diphenylamine oxide  can be obtained by freezing the dark-red reaction mixture formed on oxidation of diphenylhydroxylamine [21]. Molecular weight determination shows that diphenyl nitrogen oxide is a radical which does not associate even at very low temperatures. It reacts immediately with nitrogen oxide and triphenylmethyl forming colourless substances:



## 5-3.1 Semiquinones*

Semiquinones may serve as examples of stable free organic radicals with the unpaired electron on the oxygen.

Semiquinones are intermediate compounds in the oxidation of hydroquinones or in the reduction of quinones in alkaline solution. The following equilibrium was established for a large number of examples:

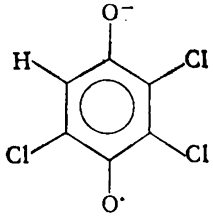


Hydroquinone ion | Quinone | Semiquinone

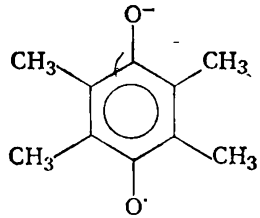
Semiquinones were studied by paramagnetic susceptibility measurements [23], potentiometric titration and absorption spectra. Especially fruitful were electronic spin resonance studies [24].

The two oxygens in the above formula are different (one carries a negative charge, the other an unpaired electron).

Actually the unshared electron (and the negative charge as well) evidently belongs to both oxygen atoms. The detailed structure of ESR spectra (for example, in the case of trichlorosemiquinone and durosemiquinone) definitely indicates considerable delocalization of the unshared electron.



Trichlorosemiquinone



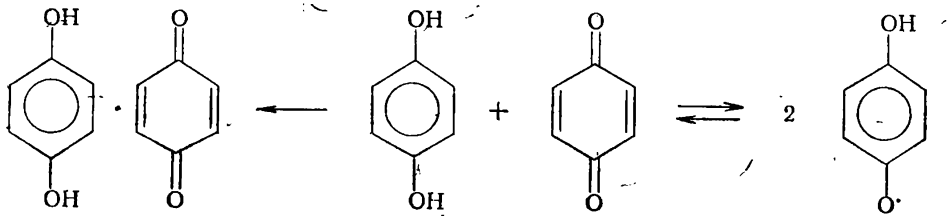
Durosemiquinone

Thus, semiquinones have a symmetrical structure and both oxygens have the same electron density.

---

* For reviews see [22].

It should be remembered that in acid solution semiquinones are unstable and the equilibrium is shifted to the left.



Quinhydrone

Molecular complexes of hydroquinones with quinones—quinhydrones—are diamagnetic.

## 5-4 ORGANOMETALLIC FREE RADICALS

Like hexaphenylethane, organometallic compounds of the $Ar_3Me - MeAr_3$ type react readily with sodium, as well as with iodine and other halogens in a number of cases.

$$(C_6H_5)_3Ge{-}Ge(C_6H_5)_3 \xrightarrow{2Na} 2(C_6H_5)_3GeNa$$

$$(C_6H_5)_3Ge{-}Ge(C_6H_5)_3 \xrightarrow{Br_2} 2(C_6H_5)_3GeBr$$

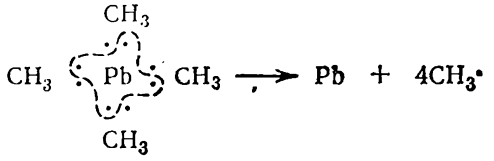
Hexaphenyldistannane $(C_6H_5)_3Sn - Sn(C_6H_5)_3$ is oxidized by atmospheric oxygen. Aliphatic organometallic compounds like hexamethyldistannane $(CH_3)_3Sn - Sn(CH_3)_3$ also react readily with oxygen, sulphur, iodine and metallic sodium. Some of the compounds mentioned have low apparent molecular weights. All these properties, apparently, indicate the possibility of dissociation into free organometallic radicals:

$$R_3Me{-}MeR_3 \rightleftarrows 2R_3Me\cdot$$

However magnetic susceptibility measurements showed [25] that all the organometallic compounds of germanium, tin and lead which were thought to be capable of dissociation into free radicals, possess only diamagnetic properties. Hence, no organometallic free radicals are known so far. The high reactivity of $R_3Me - MeR_3$ organometallic compounds may be due to the low energy of the metal-metal bond.

## 5-5 FREE ALIPHATIC RADICALS IN THE GAS PHASE*

Paneth obtained free methyl [27] and ethyl radicals [28] by heating tetramethyl- (and tetraethyl-) lead, respectively:



Owing to the presence of a localized unpaired electron on the carbon atom (and consequently to the high energy of the latter) methyl and ethyl radicals exist only 0.001 seconds and are highly reactive. At room temperature they react with different metals to form organometallic compounds:

$$4R\cdot + Pb \longrightarrow PbR_4$$
$$2R\cdot + Hg \longrightarrow R_2Hg$$
$$2R\cdot + 2Te \longrightarrow R{-}Te{-}Te{-}R$$

Reactions of free methyl and ethyl radicals with metallic arsenic result in compounds of the types $AsR_3$, $R_2As - AsR_2$, and $AsR_5$; with antimony they form compounds of the types $SbR_3$ and $R_2Sb - SbR_2$, and with bismuth, of the types $BiR_3$ and $R_2Bi{-}BiR_2$.

Thermal decomposition of tetraalkyl lead does not yield radicals larger than ethyl. For instance, no propyl or butyl radicals are formed as a result of the thermal decomposition of tetrapropyl or tetrabutyl lead. Evidently, the higher alkyl radicals decompose under the conditions of the experiment into ethyl and methyl radicals. However, these radicals, propyl in particular, exist at room temperature.

Thus, if a mixture of mercury, hydrogen and propylene vapours is exposed to ultraviolet radiation the following reaction takes place [29]:

$$Hg(6^3p) + H_2 \xrightarrow{h\nu} 2H\cdot + Hg(6^1s)$$
$$H\cdot + CH_3{-}CH{=}CH_2 \longrightarrow CH_3{-}CH_2{-}CH_2\cdot$$
$$CH_3{-}CH_2{-}CH_2\cdot + Hg \rightleftarrows CH_3{-}CH_2{-}CH_2{-}Hg\cdot$$

Besides pyrolysis and photolysis of organometallic compounds, free alkyl radicals can be obtained by pyrolysis and photolysis of a number of other organic substances.

For example, free methyl radicals can be obtained quantitatively by heating azomethane to 400°:

$$CH_3{-}N{=}N{-}CH_3 \longrightarrow N_2 + 2CH_3\cdot$$

* See [26] for details.

Free radicals form on decomposition of aldehydes or ketones by ultraviolet light, for example*:

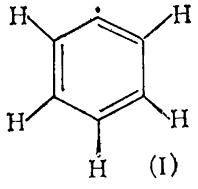
$$CH_3—CO—CH_3 \xrightarrow{h\nu} CH_3\cdot + \cdot COCH_3 \longrightarrow CH_3—CH_3 + CO$$

Photolysis of alkyl halides also results in free radicals.

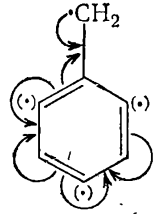
The formation of the methylene biradical on decomposition of diazomethane was proved by the method of removal of metallic mirrors: the thermal decomposition of diazomethane results in active particles which react with selenium, tellurium, arsenic or antimony mirrors. However, unlike methyl radicals, they do not remove zinc, cadmium or lead mirrors.

## 5-6 FREE AROMATIC RADICALS IN THE GAS PHASE

The phenyl free radical (I) has an unpaired electron, evidently localized largely on a single carbon atom, because it has no opportunity to delocalize this electron cloud, like the benzyl radical (II), for example:




(I)




(II)

Because of this, phenyl must have as high an energy and as short a lifetime as the methyl or ethyl radicals.

It is not surprising, therefore, that Paneth *et al.* failed to find $C_6H_5$ on pyrolysis of tin tetraphenyl, but discovered benzyl readily on pyrolysis of tin tetrabenzyl.

The phenyl radical was proved to exist for a very short time in the gas phase on photolysis of acetophenone.

## 5-7 FREE RADICALS IN THE LIQUID PHASE

### 5-7.1 Hypothesis of the Formation of Short-Lived Radicals in Solution

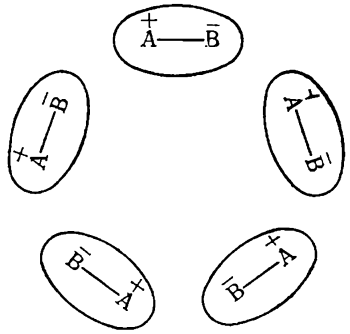
Homolytic decomposition of a single molecule, i.e., a gas particle, takes place easier than heterolytic, because in the latter case considerable energy is needed to overcome electrostatic forces.

* When carried out with aliphatic hydrocarbons, this reaction yields methane instead of ethane; the solvent loses an equivalent of hydrogen which reacts with the methyl radicals:

$$CH_3\cdot + C_nH_{2n+2} \longrightarrow CH_4 + \cdot C_nH_{2n+1}$$
$$2\cdot C_nH_{2n+1} \longrightarrow C_nH_{2n} + C_nH_{2n+2}$$

Therefore, in the majority of cases gas reactions follow a homolytic course.

It is a different thing, however, when organic reactions occur in solution where the molecules are close to each other, so that their interactions cannot be disregarded. For example, the electrical polarization of the bond A — B may be enhanced considerably owing to the formation of closed chains of polar molecules.



Thus, in dissolved substances the energy required for a heterolytic scission may be much smaller than that necessary for a homolytic break, and indeed, in the majority of cases organic reactions in solutions take place heterolytically.

However, a number of phenomena discovered by investigators studying organic reactions in solution could not be explained by ionic mechanisms. Many such phenomena became known beginning with the thirties of this century. The need to explain these facts, the number of which kept constantly growing, was responsible for the hypothesis that in some cases reactions in solutions give rise to short-lived free radicals.

As a result of numerous investigations a new field of organic chemistry arose, which may be rightfully called the chemistry of free radicals in solution.

It should be noted that the specific properties of free radicals in solution (short lifetime and mainly the simultaneous occurrence of many reactions) are responsible in most cases for the inadequacy of physicochemical methods for these investigations (for instance, measurement of magnetic susceptibility).

Thus, there are as yet no direct methods for detecting and identifying short-lived radicals existing in solutions. With the discovery of electron spin resonance (ESR or paramagnetic resonance) chemists obtained an important physical method for studying free radicals, but the ESR method is not applicable to most free radical reactions because of the extremely low concentrations of the free radicals.

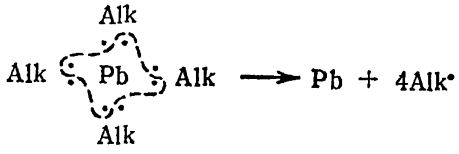
Therefore at present the main criterion of the existence of free radicals in solution and the method of studying their properties is investigation of the end products of the reactions.

For this reason the material given below on free radicals in the liquid phase will be classified according to the types of reactions in the course of which short-lived alkyl or aryl radicals are formed.

## 5-7.2 Decomposition of Organometallic Compounds

### Thermal and Photochemical Decomposition of Aliphatic Organometallic Compounds

Thermal decomposition of different elementoorganic compounds takes place at different temperatures, beginning with temperatures considerably below 0° (organocopper and organosilver compounds) and up to temperatures in excess of 500° (organosilicon compounds). For a considerable number of organometallic compounds this decomposition evidently follows the mechanism established by Paneth in the example of pyrolysis of tetramethyl and tetraethyl lead




Here the electron pairs forming the covalent bonds split to form free radicals with their odd electrons.*

Tetraalkyl lead is not so convenient a substance for the preparation of alkyl radicals in solution as in the vapour state because it does not decompose below 200°.

In the study of reactions of tetramethyl lead with liquid hydrocarbons at 200-270° it was shown that the ethyl radical hydrogenates to ethane and disproportionates to ethylene, and that a substantial amount of ethylene is converted into high-boiling hydrocarbons as a result of polymerization.

Paraffinic hydrocarbons (including cycloparaffins) and alkenes dehydrogenate readily, but aromatic hydrocarbons do not react with the ethyl radical at temperatures below 300°. Methylene and methine groups give up hydrogen more readily than the methyl group.

Alkene hydrocarbons (cyclohexene, heptene) are more likely to give up hydrogen in reactions than to form addition compounds with radicals.

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* See [30] for details of the mechanism of thermal decomposition of tetraethyl lead.

Razuvayev *et al.* [31] studied the photochemical decomposition of dimethyl mercury in organic solvents.

The primary reaction consists in split-off of one methyl group

$$CH_3:Hg\overset{\cdot\cdot}{\underset{\cdot\cdot}{\cdot}}CH_3 \xrightarrow{h\nu} CH_3—Hg\cdot + \cdot CH_3$$

That a $CH_3Hg\cdot$ radical forms is proved by its reactions with halogen-containing solvents. For example, photolysis of dimethylmercury in carbon tetrachloride results in methylmercury chloride, methyl chloride and hexachloroethane. The formation of these reaction products may be explained as follows:

$$(CH_3)_2Hg \xrightarrow{h\nu} CH_3Hg\cdot + \cdot CH_3$$
$$CH_3Hg\cdot + CCl_4 \longrightarrow CH_3HgCl + \cdot CCl_3$$
$$CH_3\cdot + CCl_4 \longrightarrow CH_3Cl + \cdot CCl_3$$
$$2\cdot CCl_3 \longrightarrow CCl_3—CCl_3$$

Photolysis of dimethylmercury in chloroform yields methylmercury chloride, hexachloroethane and methane.

In solvents which do not contain halogens, dimethylmercury decomposes further into mercury and methyl radical.

Methyl radicals formed by the photolysis of dimethylmercury do not react with benzene.

If dimethylmercury dissolved in a mixture of methanol and carbon tetrachloride is irradiated, the resulting $CH_3Hg\cdot$ and $CH_3\cdot$ radicals react selectively, each with a definite component of the solvent:

$$CH_3Hg + CCl_4 \longrightarrow CH_3HgCl + \cdot CCl_3$$
$$2\cdot CCl_3 \longrightarrow CCl_3—CCl_3$$
$$2CH_3\cdot + CH_3OH \longrightarrow 2CH_4 + CH_2O$$

The formation of such reaction products shows that the radicals $CH_3Hg\cdot$ and $CH_3\cdot$ must exist in solution as kinetically independent particles sufficiently long to collide with a molecule of the corresponding component of the solvent.

### Thermal Decomposition of Aromatic Organometallic Compounds

Razuvayev and Koton obtained [32] the first data on the formation of aryl radicals in solution in a study of the thermal decomposition of organomercury compounds.

They showed that when solutions of diphenylmercury in substances which give up hydrogen easily are boiled, benzene, metallic mercury and the product of dehydrogenation of the solvent are

always formed. Thus, the decomposition of diphenylmercury in the presence of propanol, isopropanol or benzhydrol yields benzene, mercury and propionaldehyde, acetone and benzophenone, respectively.

Razuvayev and Koton suggested further that decomposition of the phenyl derivatives of mercury, lead and tin involves the intermediate formation of a phenyl free radical which participates readily in different reactions, e.g.:

$$(C_6H_5)_2Hg \longrightarrow 2C_6H_5\cdot + Hg$$

$$2C_6H_5\cdot + CH_3-\underset{\underset{OH}{|}}{CH}-CH_3 \longrightarrow 2C_6H_6 + CH_3-\underset{\underset{O}{\|}}{C}-CH_3$$

The reaction of diphenylmercury with hydrazobenzene conducted at 150° in ligroin solution resulted in the formation of benzene, metallic mercury and azobenzene

$$C_6H_5 \overset{|}{\underset{|}{\cdot\cdot}} Hg \overset{|}{\underset{|}{\cdot\cdot}} C_6H_5 \longrightarrow 2C_6H_5\cdot + Hg$$

$$2C_6H_5\cdot + C_6H_5-\overset{H}{\overset{\cdot\cdot}{N}}-\overset{H}{\overset{\cdot\cdot}{N}}-C_6H_5 \longrightarrow$$

$$\longrightarrow 2C_6H_6 + C_6H_5-N=N-C_6H_5$$

The reaction of diphenylmercury with isoprene, butadiene, pseudobutylene and pyrrole at 250-300° incurs the evolution of metallic mercury and the formation of high-polymeric reaction products. No benzene results because the phenyl radical formed adds to the unsaturated compound, initiating chain polymerization.

The majority of the reactions cited do not apply to dibenzylmercury which most frequently yields dibenzyl. This peculiarity of dibenzylmercury is due to the relatively low free energy of the benzyl radical (in comparison with phenyl), and, therefore, to its relatively low reactivity and sufficient stability owing to which it dimerizes but does not react with the solvent.

The phenyl radical is highly reactive and reacts immediately with the solvent. That is why no diphenyl is formed.

Biaryls form when organomercuric compounds are heated in the absence of solvents

$$Ar \overset{|}{\underset{|}{\cdot\cdot}} Hg \overset{|}{\underset{|}{\cdot\cdot}} Ar \longrightarrow Ar-Ar + Hg$$

As was shown by Nesmeyanov and Borisov [33], decomposition of trichlorovinylantimony dichloride in the absence of solvent results in 1,4-dichlorobutadiene-1,3. This substance is apparently also the dimerization product of the chlorovinyl radicals formed.

$$2(CHCl=CH)_3SbCl_2 \xrightarrow{200\text{-}250^\circ}$$
$$\longrightarrow 3CH \equiv CH + CHCl=CHCl + CHCl=CH-CH=CHCl + 2SbCl_3$$

Aryl free radicals are also formed on thermal decomposition of pentaphenylphosphorus and pentaphenylantimony in solution [34]:

$$Ph_5P \longrightarrow Ph_4P\cdot + \cdot Ph$$
$$Ph_5Sb \longrightarrow Ph_4Sb\cdot + \cdot Ph$$

For example, decomposition of pentaphenylantimony in carbon tetrachloride results in tetraphenylstibonium chloride, chlorobenzene and diphenyl. The reactions may be represented by the following scheme:

$$Ph_5Sb \longrightarrow Ph_4Sb\cdot + \cdot Ph$$
$$Ph\cdot + CCl_4 \longrightarrow Ph-Cl + \cdot CCl_3$$
$$Ph_4Sb\cdot + CCl_4 \longrightarrow Ph_4SbCl + \cdot CCl_3$$
$$2CCl_3\cdot \longrightarrow CCl_3-CCl_3$$
$$2Ph\cdot \longrightarrow Ph-Ph$$

The formation of phenyl radicals of this type was confirmed with the aid of diphenylpicrylhydrazyl.

There is reason to believe that homolytic rupture of carbon-metal bonds occurs in very many exchange reactions of organometallic compounds with metals (and with some nonmetals) which take place on prolonged heating. A number of such reactions was discovered by Kocheshkov and Talalayeva [35].

$$2C_6H_5Li + Mg \longrightarrow (C_6H_5)_2Mg + 2Li$$
$$2C_6H_5Li + Hg \longrightarrow (C_6H_5)_2Hg + 2Li$$
$$4C_6H_5Li + Sn \longrightarrow (C_6H_5)_4Sn + 4Li$$
$$4C_6H_5Li + Pb \longrightarrow (C_6H_5)_4Pb + 4Li$$
$$3C_6H_5Li + As \longrightarrow (C_6H_5)_3As + 3Li$$
$$3C_6H_5Li + Sb \longrightarrow (C_6H_5)_3Sb + 3Li$$

Many similar reactions, particularly characteristic of organomercury compounds, have been known for a long time. They form the basis of one of the most important methods of synthesis of organo-

metallic compounds:

$$R_2Hg + 2Li(Na) \longrightarrow 2RLi(Na) + Hg$$
$$R_2Hg + Be \longrightarrow R_2Be + Hg$$
$$R_2Hg + Mg \longrightarrow R_2Mg + Hg$$
$$R_2Hg + Zn \longrightarrow R_2Zn + Hg$$
$$3R_2Hg + 2Al \longrightarrow 3R_3Al + 3Hg$$
$$2RHgCl + Sn \longrightarrow R_2SnCl_2 + 2Hg$$
$$2R_2Hg + Sn \longrightarrow R_4Sn + 2Hg$$
$$3(C_6H_5)_2Hg + 2Sb \longrightarrow 2(C_6H_5)_3Sb + 3Hg$$
$$3(C_6H_5)_2Hg + 2Bi \longrightarrow 2(C_6H_5)_3Bi + 3Hg$$
$$Ar_2Hg + 2S \longrightarrow Ar_2S + HgS$$
$$Ar_2Hg + 2Se \longrightarrow Ar_2Se + HgSe$$
$$Ar_2Hg + 2Te \longrightarrow Ar_2Te + HgTe$$
$$(C_6H_5)_4Sn + 5S \longrightarrow 2(C_6H_5)_2S_2 + SnS$$
$$(C_6H_5)_4Pb + 5S \longrightarrow 2(C_6H_5)_2S_2 + PbS$$
$$(C_6H_5)_4Pb + 2Hg \longrightarrow 2(C_6H_5)_2Hg + Pb$$

It should be taken into consideration that in by no means all the above-mentioned homolytic reactions are radicals formed as kinetically independent particles.

At least for the homolytic isotope exchange reactions of the following types:

(a) $Ar_2Hg + {}^{\bullet}{}^{203}Hg\cdot \rightleftarrows Ar_2Hg^{203} + \cdot Hg\cdot$

(b) $Ar-Hg-X + {}^{\bullet}{}^{203}Hg\cdot \rightleftarrows Ar-Hg^{203}-X + \cdot Hg\cdot$

(c) $RR'R''C-Hg-X + {}^{\bullet}{}^{203}Hg\cdot \rightleftarrows RR'R''C-Hg^{203}-X + \cdot Hg\cdot$

it has been proved definitely [36-40] that free radicals are not formed. These reactions proceed easily under such mild conditions which exclude the possibility of thermal decomposition of organomercury compounds to form free radicals. The reaction of type (c) involves strict retention of configuration at the asymmetric carbon atom. Finally, if the isotopic exchange takes place between unsymmetrical diarylmercury and radioactive mercury, only the radioactive unsymmetrical compound forms,

$$Ar-Hg-Ar' + Hg^{203} \rightleftarrows Ar-Hg^{203}-Ar' + Hg$$

with no disproportionation products ($Ar_2Hg^{203}$ and $Ar'_2Hg^{203}$).

Hein and coworkers [41] think that neutral phenyl radicals form during the decomposition of pentaphenyl chromium salts $(C_6H_5)_5CrX$, which are strong reducing agents and easily lose one phenyl group.

The metallation reactions with dimethylmercury and diphenylmercury, studied by Koton [42],

$$(CH_3)_2Hg + RC_6H_4OH \longrightarrow CH_4 + CH_3HgC_6H_3(OH)R$$
$$(C_6H_5)_2Hg + RC_6H_4OH \longrightarrow C_6H_6 + C_6H_5HgC_6H_3(OH)R$$

are most probably also homolytic processes, which confirms the formation of 3-methylmercury-4-nitrophenol in the reaction of dimethylmercury with *p*-nitrophenol. If this reaction were not radical but electrophilic, 2-methylmercury-4-nitrophenol would have been expected to form in accordance with the rules of orientation in reactions of electrophilic substitution in the benzene ring.

### Photochemical Decomposition of Organometallic Compounds of the Aromatic Series

Photochemical reactions of aromatic organometallic, predominantly organomercury, compounds were studied thoroughly by Razuvayev and coworkers.

Photochemical reactions of organomercury compounds of the $Ar_2Hg$ type with alcohols proceed according to the equation

$$Ar_2Hg + RCH_2OH \xrightarrow{h\nu} 2ArH + Hg + R-C\begin{matrix}=O\\ \diagdown H\end{matrix}$$

i.e., the course of the reaction is the same as that of thermal reactions of diarylmercury with alcohols.

The photochemical reactions of diphenylmercury with 2,2,4-trimethylpentane, toluene, ethyl ether, ethylcellosolve, acetone and ethyl formate result in benzene and metallic mercury in all cases. Reactions with different solvents show a wide difference in reaction rates.

It is known that diphenyl- and ditolylmercury do not react with halogen derivatives of hydrocarbons even if reaction mixtures are refluxed for days. The reaction does not take place even when diphenylmercury is heated with chloroform or bromoform in sealed tubes at 130°; only iodoform reacts with diphenylmercury to form benzene, phenylmercuric iodide and tetraiodoethylene. This inertness of organomercury compounds is apparently attributable to the fact that under the conditions of the reaction no cleavage of the aryl-metal bond to form aryl radicals takes place, because the latter react easily with the halogen derivatives of hydrocarbons (pages 372, 377).

In contrast, diarylmercury reacts readily with the halogen derivatives of hydrocarbons when the reaction mixture is exposed

to ultraviolet light. Photolysis of diphenylmercury in carbon tetrachloride results in phenylmercuric chloride, chlorobenzene and hexachloroethane. The reaction evidently proceeds according to the following mechanism:

$$(C_6H_5)_2Hg \xrightarrow{h\nu} C_6H_5{-}Hg\cdot + \cdot C_6H_5$$
$$C_6H_5Hg\cdot + CCl_4 \longrightarrow C_6H_5{-}HgCl + \cdot CCl_3$$
$$C_6H_5\cdot + CCl_4 \longrightarrow C_6H_5Cl + \cdot CCl_3$$
$$2\cdot CCl_3 \longrightarrow CCl_3{-}CCl_3$$

Diphenylmercury reacts photochemically with trichloroethylene easily, forming phenylmercuric chloride and benzene, whence it follows that the presence of a double bond at the carbon to which the halogen is linked has no effect on the reaction rate. It is interesting that tertiary butyl chloride, which possesses a rather mobile chlorine atom in nucleophilic reactions, reacts very slowly with diphenylmercury on irradiation [43].

Other diaryl compounds of mercury (ditolylmercury, dinaphthylmercury, etc.) behave like diphenylmercury in photochemical reactions.

Arylmercuric halides do not decompose even after prolonged irradiation. Unlike them, phenylmercuric hydroxide reacts easily with different solvents on irradiation. Judging from the nature of the products formed, the first stage consists in photolysis of $C_6H_5HgOH$ into free radicals:

$$C_6H_5 : Hg \overset{\vdots}{\underset{\vdots}{\cdot\cdot}} OH \xrightarrow{h\nu} C_6H_5Hg\cdot + \cdot OH$$

The resulting hydroxyl radical always removes a hydrogen from the solvent to form water. The $C_6H_5Hg\cdot$ radical reacts with solvents exactly like in photochemical reactions of diphenylmercury.

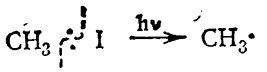
### 5-7.3 Reactions of Alkyl Halides with Metals

Reactions of alkyl halides with metals involving a stage wherein neutral radicals are formed and resulting in organometallic compounds, have been known for a long time. However, their mechanism could be elucidated correctly only relatively recently due to the progress attained in the chemistry of short-lived free radicals.

In 1850 Frankland [44] noticed that ethyl iodide reacts with metallic mercury to form gaseous reaction products. Two years later he discovered [45], that methyl iodide also reacts with metallic mercury, forming methylmercuric iodide. This reaction proceeds faster in sunlight. Ethylmercuric iodide could not be prepared in this way; instead, in the reaction of ethyl iodide with mercury in sunlight mercurous iodide, ethane and ethylene are formed.

The remarkable reaction of alkyl iodides with metallic mercury, which at one time attracted the attention of many chemists, may be explained at present as follows.

Under the influence of light the carbon-iodine bond undergoes homolytic cleavage to form an alkyl free radical and atomic iodine:



The alkyl radical reacts with metallic mercury forming a free radical with an odd electron at the mercury atom (see page 374):

$$CH_3\cdot + \cdot Hg\cdot \longrightarrow CH_3{-}Hg\cdot$$

The latter attacks another molecule of alkyl iodide abstracting an iodine atom from it and freeing another alkyl radical, capable of continuing the chain reaction:

The failure of attempts to prepare ethylmercuric iodide under the above conditions is due to the fact that this compound is decomposed by direct sunlight.

Ethylmercuric iodide can be obtained by illuminating a mixture of ethyl iodide and metallic mercury with scattered light which, of course, does not decompose the organomercury compound.

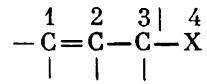
In 1855 Zinin [46] found that if a mixture of allyl iodide is shaken with mercury, a good yield (80-90%) of alkylmercuric iodide rapidly results.

$$CH_2{=}CH{-}CH_2{-}I + Hg \longrightarrow CH_2{=}CH{-}CH_2{-}HgI$$

Not only does this reaction not require illumination with sunlight, but the allyl iodide even has to be diluted with ethanol to avoid too vigorous a reaction.

The ease of reaction between allyl iodide and metallic mercury is due to the following.

It is known that in systems of the type:



the reactivity of the C — X bond (3, 4) is enhanced owing to its conjugation with the C = C bond (1, 2). This increased reactivity is exhibited, in particular, in reactions accompanied by homolytic cleavage of the C — X bond.

In the allyl iodide molecule homolytic cleavage of the carbon-iodine bond would be expected to occur readily under the influence

of various factors (sunlight, collision with mercury atoms, etc.). This makes it possible for a large number of allyl radicals to form in the reaction mixture, capable of initiating a chain reaction of allyl iodide with mercury.

The availability of a large number of chains naturally shortens the time necessary for the reaction.

The reaction of methylene iodide and iodoform with metallic mercury in a sealed tube in the presence of mercurous iodide results in organomercury compounds:

$$CH_2I_2 + Hg + (Hg_2I_2) \longrightarrow ICH_2HgI + (Hg_2I_2)$$
$$CH_2I_2 + 2Hg + (Hg_2I_2) \longrightarrow IHg{-}CH_2{-}HgI + (Hg_2I_2)$$

Apparently, in this reaction mercurous iodide serves as a source of reactive finely dispersed metallic mercury

$$Hg_2I_2 \xrightarrow[\text{(sunlight)}]{h\nu} 2Hg + \; I_2$$
$$\downarrow CH_2I_2 \qquad \downarrow 2Hg$$
$$ICH_2HgI \qquad Hg_2I_2$$

Iodoform reacts readily with metallic mercury in the sunlight in ethanol solution forming triply mercuriated methane:

$$CHI_3 + 3Hg \xrightarrow{h\nu} H{-}C(HgI)_3$$

There is hardly any doubt that the above two reactions proceed through a stage where free radicals are formed as a result of photolysis or thermal decomposition of the iodine derivative, for example:

$$CHI_3 \longrightarrow \cdot CHI_2 + \cdot I$$

$$2\cdot I + 2Hg \longrightarrow Hg_2I_2$$

$$I_2HC\cdot + Hg \longrightarrow I_2HC{-}Hg\cdot$$

$$I_2HC{-}Hg\cdot + I{:}CHI_2 \longrightarrow I_2HC{-}HgI + \cdot CHI_2 \text{ etc.}$$

Trifluoroiodomethane reacts with mercury when irradiated with ultraviolet light forming trifluoromethylmercuric iodide. The reaction proceeds through the stage of formation of a trifluoromethyl

free radical:

$$F_3C\text{:}I \xrightarrow{h\nu} F_3C\cdot + \cdot I$$

$$F_3C\cdot + Hg \longrightarrow F_3C{-}Hg\cdot$$

$$F_3C{-}Hg\cdot + I\text{:}CF_3 \longrightarrow F_3C{-}HgI + \cdot CF_3, \text{ etc.}$$

Maynard [47] studied in detail the mechanism of the reaction between methyl iodide and mercury. He established that in carrying out the reaction $CH_3I + Hg \xrightarrow{h\nu} CH_3 - Hg - I$ it took from 3 to 10 hours in each case for methylmercuric iodide to appear in the reaction mixture. In all cases mercurous iodide forms first and only then does methylmercuric iodide begin to form at a measurable rate.

The role of mercurous iodide thus consists in that it decomposes photochemically into finely divided metallic mercury which reacts with the alkyl iodide:

$$Hg_2I_2 \xrightarrow{h\nu} Hg + HgI_2$$

For a long time it was accepted that with the exception of bromobenzyl cyanide, alkyl bromides and aromatic iodine derivatives do not react with metallic mercury. However, it was discovered [48] that bromoderivatives in whose molecules the carbon-bromine bond is activated by conjugation with a double bond

$$\left(>C{=}C{-}\underset{|}{C}{-}Br \quad \text{or} \quad O{=}\underset{|}{C}{-}\underset{|}{C}{-}Br\right)$$

are capable of reacting with metallic mercury, giving good yields of organomercury compounds of the R—HgBr type in some cases.

The reaction of bromoderivatives with metallic mercury is a convenient method of synthesizing optically active organomercury compounds with mercury at the asymmetric carbon atom [49]:

$$\begin{matrix} R \\ R'{-}\overset{*}{C}{-}Br \\ R'' \end{matrix} + Hg \longrightarrow \begin{matrix} R \\ R'{-}C{-}HgBr \\ R'' \end{matrix}$$

The reaction of bromoform and carbon tetrachloride with metallic mercury is accelerated by the presence of benzoyl peroxide (in agreement with the hypothesis of the radical nature of these reactions), but does not result in organometallic compounds.

Thus, the reaction of carbon tetrachloride with mercury in the presence of benzoyl peroxide at reflux in $CCl_4$ proceeds according to the equation:

$$2CCl_4 + 2Hg \longrightarrow CCl_3{-}CCl_3 + Hg_2Cl_2$$

The reaction of alkyl chlorides and bromides ($CCl_4$, $CHCl_3$, $CHBr_3$, $CH_2 = CH-$ $-CH_2Br$) with mercury is also accelerated by irradiation with ultraviolet light.

Tin, lead, antimony, and certain other metals are capable of reacting with alkyl halides (iodides, and sometimes bromides), yielding organometallic derivatives.

The action of tin on alkyl iodides, in some cases in the sunlight at ordinary temperature, in others at 150-180°, results in mixtures of $R_2SnI_2$ and $R_3SnI$. The reaction proceeds more smoothly with alkyl bromides.

$$2RBr + Sn \longrightarrow R_2SnBr_2$$

Kocheshkov showed [50] that when tin is heated with methylene bromide tribromomethyl tin and carbon are formed.

$$3CH_2Br_2 + Sn \longrightarrow 2CH_3SnBr_3 + C$$

Methylene chloride practically does not react with metallic tin, even after 120 hours' heating (at 185-220°). Methylene iodide forms tin tetraiodide under similar conditions.

Finely ground arsenic reacts with an excess of alkyl iodide at 150-200° in a sealed tube to form a double compound of tetraalkylarsonium iodide and arsenic triiodide

$$4RI + As \longrightarrow R_4AsI \cdot AsI_3$$

Amorphous arsenic, which possesses a large surface area, reacts with methyl iodide even in the cold or at the temperature of a water bath forming methyldiiodoarsine, cacodyl iodide, trimethylarsine and arsenic triiodide. Amorphous arsenic reacts with iodoform violently with a flash; in benzene solution the reaction proceeds more tranquilly, forming diiodomethyldiiodoarsine $CHI_2AsI_2$ and bis-diiodomethyliodoarsine iodide $(CHI_2)_2AsI$.

The reaction of amorphous arsenic with chloroform, carbon tetrachloride, dichloro- and dibromoethane does not result in organometallic compounds of arsenic.

If heated rapidly to 140° in a sealed tube with alkyl halides finely pulverized metallic antimony forms mainly dihalotrialkylantimony, $R_3SbX_2$.

Like the reactions of alkyl halides with mercury, the reactions of alkyl halides with tin, arsenic and antimony are apparently homolytic in nature.

### Decarbonylation of Aldehydes and Ketones

Alkyl free radicals are formed on photochemical decomposition of aldehydes and ketones.

$$R-\underset{\underset{O}{\|}}{C}-R \xrightarrow{h\nu} R-\underset{\underset{O}{\|}}{C}\cdot + \cdot R \longrightarrow R-R + CO$$

Aldehydes can be decarbonylated in the presence of peroxides (for example, *tert*-butyl peroxide) to form free radicals:

$$R-\overset{H}{\underset{|}{C}}=O \xrightarrow{t\text{-}C_4H_9O\cdot} t\text{-}C_4H_9OH + R-\dot{C}=O$$

$$R-\dot{C}=O \longrightarrow R\cdot + CO$$

$$R\cdot + R-\overset{H}{\underset{|}{C}}=O \longrightarrow R-H + R-\dot{C}=O \text{ etc.}$$

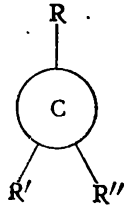
Doering showed [51] that decarbonylation of an optically active aldehyde at the asymmetric carbon atom results in the formation of a racemic hydrocarbon, e.g.:

$$(CH_3)_3C-\overset{CH_3}{\underset{C_2H_5}{\overset{|}{\underset{|}{C^*}}}}-CHO \xrightarrow{(CH_3)_3CO\cdot} (CH_3)_3C-\overset{CH_3}{\underset{C_2H_5}{\overset{|}{\underset{|}{C}}}}-\dot{C}=O \xrightarrow{-CO}$$

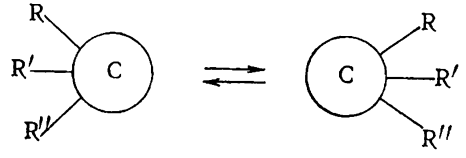
$$\longrightarrow (CH_3)_3C-\overset{CH_3}{\underset{C_2H_5}{\overset{|}{\underset{|}{C}}}}\cdot \xrightarrow{RCHO} (CH_3)_3C-\overset{CH_3}{\underset{C_2H_5}{\overset{|}{\underset{|}{C}}}}-H + R\dot{C}O$$

Racemic

This fact agrees with the proofs given above to the effect that alkyl free radicals do not retain configuration, either because of all three bonds being located in one plane

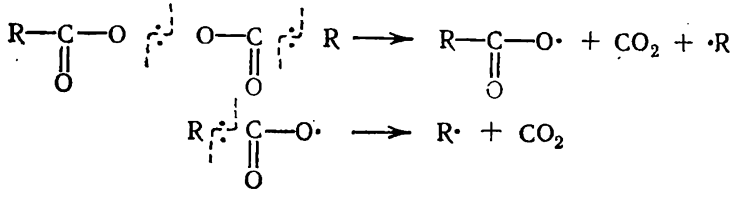



or because of rapid transformations of trigonal configurations:



### 5-7.4 Thermal Decomposition of Diacyl Peroxides

The thermal and photochemical decomposition of diacyl peroxides proceeds according to the scheme:



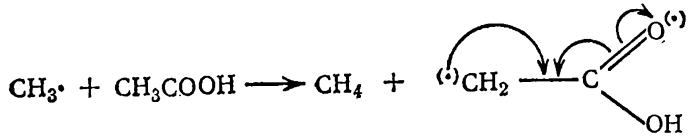
Photochemical decomposition of acetyl peroxide in the vapour phase results in ethane, carbon dioxide and a small amount of methane, while photolysis of pure liquid acetyl peroxide and its solutions in cyclohexane or ethanol yields more methane than ethane. Thus, methyl radicals dimerize in the gas phase, but in the liquid phase they mainly remove hydrogen from the solvent.

When acetyl peroxide is refluxed in toluene, 50% of methane and 2% of ethane are formed. Prolonged boiling of acetyl peroxide in acetic acid or in acetic anhydride gives carbon dioxide, succinic acid (50% yield) and methyl acetate (5% yield).

The formation of methyl acetate is probably due to the scheme:

$$CH_3CO{-}O{-}O{-}COCH_3 \longrightarrow CH_3\cdot + CO_2 + \cdot O{-}COCH_3$$
$$CH_3\cdot + \cdot O{-}CO{-}CH_3 \longrightarrow CH_3OCOCH_3$$

Succinic acid apparently forms as a result of the reaction of acetic acid with the methyl free radical and subsequent dimerization of the $\cdot CH_2COOH$ radical, which exists for a relatively long time because of the possibility of delocalization of the cloud of the unpaired electron between the carbon and the oxygen atoms:

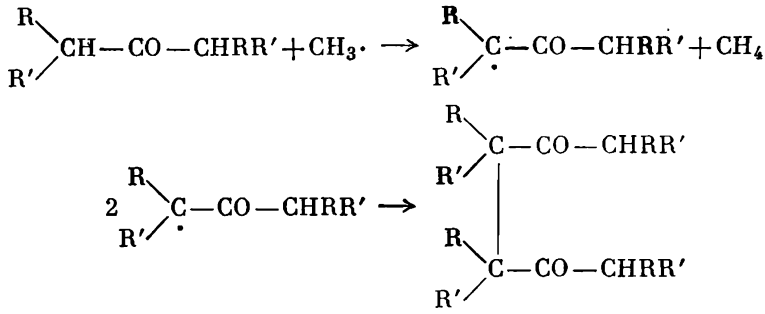


$$2 \cdot CH_2COOH \longrightarrow HOOC{-}CH_2{-}CH_2{-}COOH$$

Similarly, when acetyl peroxide was decomposed in isobutyric and chloroacetic acids, tetramethylsuccinic and dichlorosuccinic acids were found among reaction products.

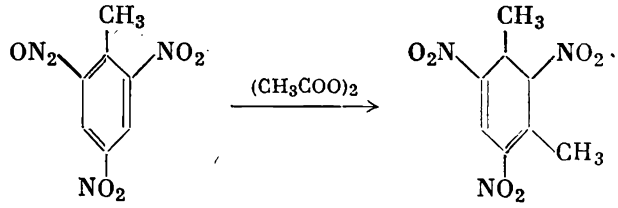
Kharasch and coworkers investigated in detail a number of cases of the decomposition of acetyl peroxide, where the mobile hydrogen was removed from a solvent molecule resulting in the formation of dimeric products [52].

For example, the decomposition of acetyl peroxide in aliphatic ketones was utilized by him for the synthesis of 1,4-diketones:

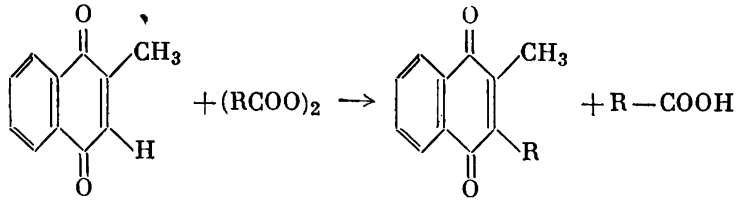


Although free radicals react with benzene with difficulty, they may replace hydrogen in some aromatic systems.

Fieser and others [53] have shown that trinitroxylene may be prepared in 10% yield by prolonged reflux of acetyl peroxide with trinitrotoluene in glacial acetic acid.



In a like manner *m*-dinitrobenzene gives a mixture of 2,4-dinitrotoluene and 2,4-dinitro-*m*-xylene. Quinones can easily be alkylated by this method. The reaction may be carried out with a large number of acyl peroxides (R = $CH_3$, *n*-$C_{15}H_{31}$, *n*-$C_{17}H_{35}$, etc.) [54].



Even alkenyl radicals may be substituted into the quinoid ring, which indicates the possibility of such short-lived radicals.

Nesmeyanov and coworkers have shown [55] that the trichloromethyl radical is evidently capable of replacing hydrogen in certain aromatic systems.

The reaction of acyl peroxides with metallic mercury was studied by Razuvayev and coworkers [56, 57].

When a mixture of metallic mercury, carbon tetrachloride and benzoyl peroxide is heated, phenylmercuryl chloride results, though in a very insignificant yield. The reaction apparently follows the following mechanism:

$$(C_6H_5COO)_2 \longrightarrow C_6H_5\cdot + CO_2 + \cdot OCOC_6H_5$$
$$C_6H_5\cdot + \cdot Hg\cdot \longrightarrow C_6H_5-Hg\cdot$$
$$C_6H_5-Hg\cdot + CCl_4 \longrightarrow C_6H_5-HgCl-\cdot CCl_3$$
$$2\cdot CCl_3 \longrightarrow CCl_3-CCl_3$$

When acetyl peroxide is heated with mercury in benzene, methylmercuric acetate results, which can be isolated as methylmercuric iodide in a 65% yield:

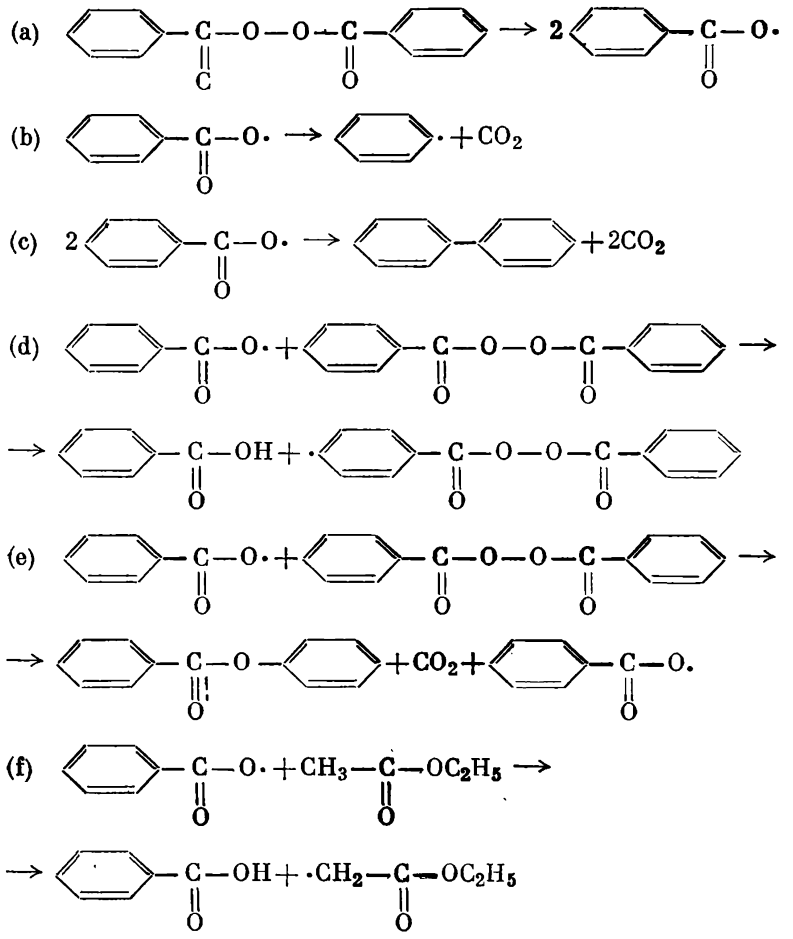
$$(CH_3COO)_2 \longrightarrow CH_3^{\bullet} + CO_2 + {}^{\bullet}OCOCH_3$$
$$CH_3^{\bullet} + Hg + {}^{\bullet}OCOCH_3 \longrightarrow CH_3-Hg-OCOCH_3$$
$$CH_3-Hg-OCOCH_3 \xrightarrow{KI} CH_3-Hg-I$$

Such a high yield of an organomercury compound is apparently ascribed to the fact that methyl radicals do not react with benzene at temperatures below 300°, so that practically no side reaction occurs between the acetyl peroxide and the solvent.

When benzoyl peroxide is used instead of acetyl peroxide, the side reaction with the solvent becomes noticeable; however, even in this case the yield of the organomercury compound is 31.5%.

$$(C_6H_5COO)_2 + Hg \longrightarrow \begin{array}{l} C_6H_5-Hg-OCOC_6H_5 + CO_2 \\ \quad\quad\quad\

gested the following radical-chain mechanism of its decomposition:



The formation of the main reaction products—diphenyl, carbon dioxide, benzoic acid—is due to the competing reactions: radical recombination (c) and the chain reactions (e) and (f).

Benzoyl peroxide oxidizes ethanol to acetaldehyde, but when it was decomposed in isobutanol, isobutyl benzoate and *o*- and *p*-butoxybenzoic acids were isolated (as well as benzene and isobutyraldehyde), indicating that the butoxy radical is capable of replacing hydrogen in the aromatic nucleus.

Wieland and coworkers [59] obtained proof of the formation of aryl free radicals from aromatic solvents when benzoyl peroxide is decomposed in them. They found that the action of benzoyl peroxide on triphenylmethyl results in the formation of a certain

amount of tetraphenylmethane in benzene solution:

$$C_6H_5-\underset{\underset{O}{\|}}{C}-O-O-\underset{\underset{O}{\|}}{C}-C_6H_5 \longrightarrow C_6H_5\cdot + CO_2 + \cdot O-\underset{\underset{O}{\|}}{C}-C_6H_5$$

$$C_6H_5\cdot + \cdot C(C_6H_5)_3 \longrightarrow C_6H_5-C(C_6H_5)_3$$

However, the reaction is not so simple because the solvent also participates:

$$C_6H_5-\underset{\underset{O}{\|}}{C}-O\cdot + C_6H_5 \longrightarrow C_6H_5-\underset{\underset{O}{\|}}{C}-OH + \cdot C_6H_5$$

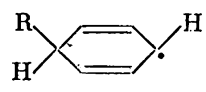
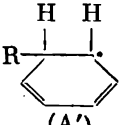
evidence of this being that tetraphenylmethane forms even if *p*-phenylbenzoyl peroxide is used instead of benzoyl peroxide.

The decomposition of benzoyl peroxide in aromatic solvents has been studied quite thoroughly. The reaction products include benzoic acid, carbon dioxide, substituted phenyl benzoates, polyphenyls and considerable quantities of tar [60].

Three possible versions of the reactions of the radicals formed on decomposition of peroxides ($C_6H_5\cdot$ and $C_6H_5COO\cdot$) with the aromatic solvent were considered:

(I) $R\cdot + C_6H_6 \longrightarrow R-C_6H_5 + H\cdot$

(II) $R\cdot + C_6H_6 \longrightarrow R-H + \cdot C_6H_5$

(III) $R\cdot + C_6H_6 \longrightarrow$  or 

(A) (A′)

Version I is the least probable, because this reaction is highly endothermic. Version II is only slightly endothermic but evidently does not take place either. This is evidenced by the fact that decompositions of benzoyl peroxide in such solvents as chlorobenzene result only in monosubstituted diphenyls. If the reaction proceeded according to variant II, disubstituted diphenyls would form along with RH.

$$R\cdot + C_6H_5-Cl \longrightarrow R-H + \cdot C_6H_4-Cl$$

$$\cdot C_6H_4-Cl + C_6H_5-Cl \longrightarrow C_6H_5-Cl + \cdot C_6H_4-Cl$$

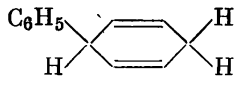
$$2\cdot C_6H_4-Cl \longrightarrow Cl-C_6H_4-C_6H_4-Cl$$

Thus the radical reacts with the aromatic solvent according to scheme III.

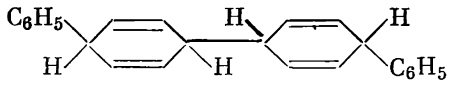
The energetics of this process is unknown, but it is reasonable to assume that the energy consumed to destroy the stable π-electron system of the benzene ring may be compensated due to the forma-

tion of a radical with a new C—C bond and an odd electron in the allyl position (A or A').

Recently dihydrophenyl (B) and tetrahydrodiphenyl (C) [61] were isolated from the products of the reaction between benzoyl peroxide and benzene:



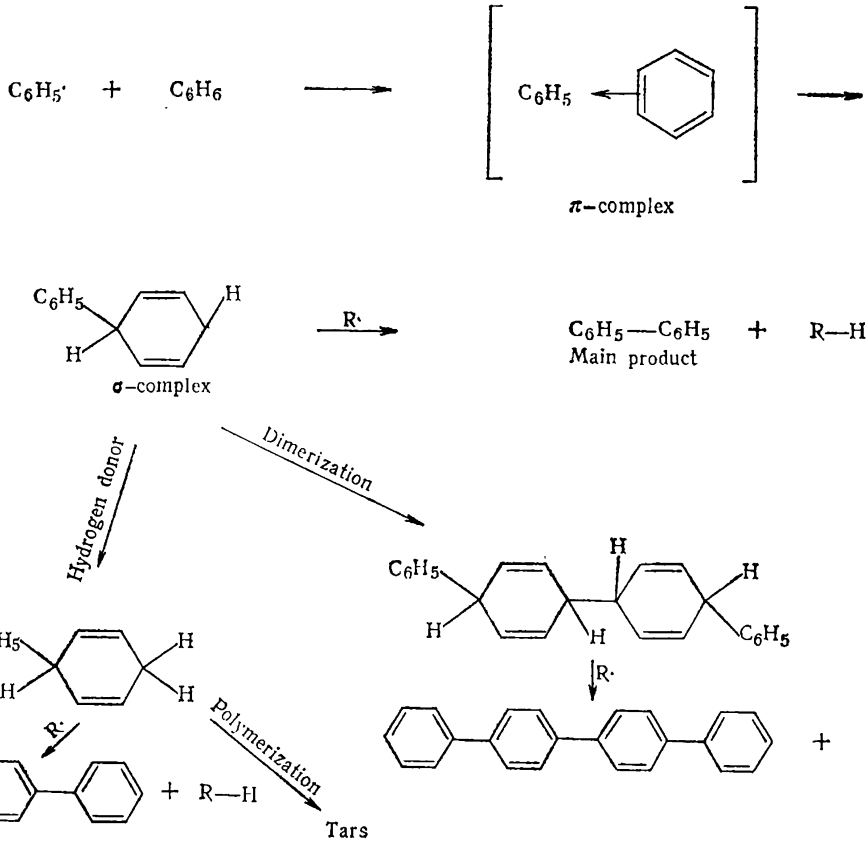

(B)



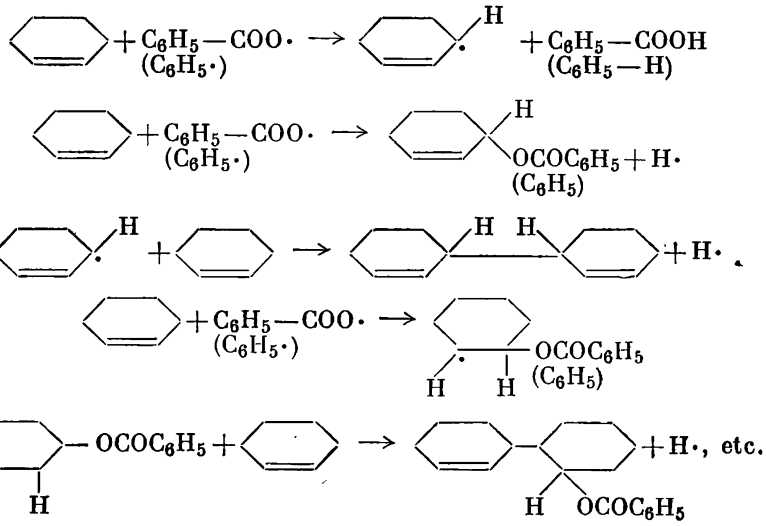

(C)

Substance (B) formed apparently as a result of hydrogenation of radical (A), and (C) by dimerization of radical (A).

Taking this into consideration, as well as the results of investigations with the use of labeled atoms [62], the general course of reaction between benzoyl peroxide and benzene may be depicted by the following scheme:



The structure of the diphenyls formed in aromatic solvents was studied by a number of investigators [63]. An extremely complex mixture results when aromatic peroxides decompose in the presence of alkenes. Farmer and Michael [64] showed that the decomposition of benzoyl peroxide in cyclohexene involves the following reactions:




Evidently, the point of attack of the free radicals on the system $-\overset{\alpha}{C}H_2-CH=CH_2$ is predominantly at the α-methylene group and not at the double bond. This is very important in the chemistry of oxidation and polymerization processes.

Organic peroxides cause polymerization of unsaturated compounds.

When benzoyl peroxide is heated to 140° with crude rubber, a certain type of vulcanization takes place; under similar conditions many diazo compounds are apparently active vulcanizers.

Rather interesting investigations were carried out by Medvedyev *et al.* [65], who obtained a number of new facts confirming the hypothesis of the radical nature of macropolymerization processes.

Studying the polymerization of chloroprene under the action of organic peroxides (benzoyl peroxide, tetralin hydroperoxide) they proved the presence of free radicals by the formation of iodine from hydrogen iodide

$$R-CH_2\cdot + HI \rightarrow R-CH_3 + I$$

and by the addition of iodine

$$R-CH_2\cdot + \cdot I \rightarrow R-CH_2-I$$

During the polymerization of chloroprene the number of free radicals increases progressively. Medvedyev and his coworkers believe that the reason for the accumulation of free radicals is the great increase in viscosity of the medium, which inhibits, and at some stages prevents, reactions of radicals with each other.

When benzoyl peroxide is refluxed with carbon tetrachloride, the formation of chlorobenzene, ω-trichloro-*p*-toluic acid and hexachloroethane takes place.

In chloroform solution the following compounds were detected: benzene, ω-trichloro-*p*-toluic acid and phosgene.

These results indicate that the solvent forms the trichloromethyl radical:

$$C_6H_5\cdot + CCl_4 \longrightarrow C_6H_5{-}Cl + \cdot CCl_3$$

$$C_6H_5\cdot + CHCl_3 \longrightarrow C_6H_5{-}H + \cdot CCl_3$$

The decomposition products of α-naphthoyl peroxide in carbon tetrachloride are: carbon dioxide, α-chloronaphthalene, α-naphthoic acid, naphthalene-1,4-dicarboxylic acid, 4-α-naphthoyl-α-naphthoic acid and hexachloroethane.

When benzoyl peroxide is decomposed in boiling tetrachloroethylene, chlorobenzene and α,β,β-trichlorostyrene are formed. This indicates the possibility of formation of the $ClC = CCl_2$ radical.

### 5-7.6 Decomposition of Organic Salts of Heavy Metals

When lead tetraacetate is heated with nitrobenzene, nitrotoluenes result. Under these conditions dinitrobenzene is methylated to dinitrotoluenes or dinitroxylenes, and naphthalene, anthracene and benzopyrene yield the corresponding acetoxy derivatives $Ar - O - COCH_3$.

The formation of all these products is apparently due to reactions of the radicals $CH_3\cdot$ and $\cdot OCOCH_3$ formed by the thermal decomposition of lead tetraacetate:

$$Pb(CH_3COO)_4 \longrightarrow Pb(CH_3COO)_2 + 2CH_3COO\cdot$$

$$CH_3COO\cdot \longrightarrow CH_3\cdot + CO_2$$

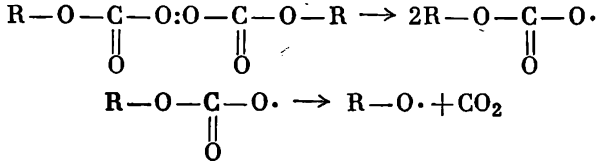
The decomposition (photochemical or thermal in the presence of peroxides) of mercuric salts of organic acids is also of a free-radical nature. The reaction of decomposition of mercuric salts may be utilized for the synthesis of organomercuric compounds [66]:

$$(R{-}COO)_2Hg \longrightarrow R{-}Hg{-}OCOR + CO_2$$

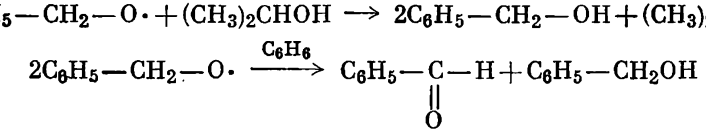
### 5-7.7 Thermal Decomposition of Percarbonates

Percarbonates are a convenient source of obtaining simple oxygen-containing radicals of the $R - O\cdot$ type in the gas phase or in solution [67]. The thermal decomposition of percarbonates follows

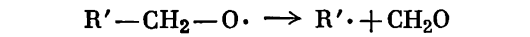
the scheme:



The R—O· radicals dehydrogenate solvent molecules or disproportionate, depending on the nature of the solvent, for example:



In many cases radicals of the R—O· type decompose into an aldehyde and an alkyl radical [68], e.g.:



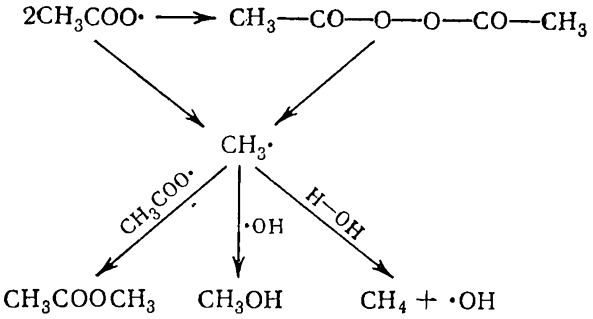
## 5-7.8 Electrolytic Preparation of Free Radicals

### Kolbe Reaction

When sodium acetate is electrolyzed, ethane and carbon dioxide form at the anode. For a long time this phenomenon was attributed to rapid discharge of the anion and dimerization of the methyl radicals.

However the formation, in some cases, of methane, methyl acetate and methyl alcohol as by-products could not be explained.

At present all the peculiarities of the Kolbe reaction can be explained by characteristic reactions of carboxylic radicals:



The formation of free radicals in the Kolbe reaction is confirmed by methylation of toluene in the anodic cell [69] and also by the substitution that occurs in the pyridine ring [70] when the electrolysis is carried out in pyridine solution.

### Electrolysis of Aliphatic Organometallic Compounds

Electrolysis of organometallic compounds of alkali metals produces free radicals at the anode. For instance, the electrolysis of ethylsodium (in diethylzinc as solvent) with a lead anode results in tetraethyl lead; the gaseous products of the reaction are ethane and ethylene.

Similar results are obtained when organomagnesium compounds are electrolyzed in ethers [71].

(a) Electrolysis of propylmagnesium bromide in ethyl ether results in the following gaseous products: propane, propylene, ethylene and carbon dioxide; the reaction products in the electrolyte solution are: hexane, ethanol, propanol and secondary amyl alcohol:

$$C_3H_7\cdot + C_2H_5-O-C_2H_5 \longrightarrow C_3H_8 + CH_3-\underset{\cdot}{CH}-O-C_2H_5$$

$$CH_3-\underset{\cdot}{CH}-O-C_2H_5 \longrightarrow CH_3-CHO + C_2H_5\cdot$$

$$CH_3-CHO + C_3H_7MgBr \longrightarrow CH_3-CH(OH)-CH_2-CH_2-CH_3$$

$$2C_2H_5\cdot \longrightarrow C_2H_6 + C_2H_4$$

(b) Electrolysis of methylmagnesium iodide in di-*n*-butyl ether results in abstraction of hydrogen from the α- and β-positions by methyl radicals:

(1) $CH_3\cdot + C_4H_9O-CH_2-CH_2-C_2H_5 \longrightarrow CH_4 + C_4H_9O-\underset{\cdot}{CH}-C_3H_7$

$$C_4H_9O-\underset{\cdot}{CH}-C_3H_7 \longrightarrow n\text{-}C_4H_9\cdot + C_3H_7CHO$$

$$\downarrow \qquad \downarrow \text{CH}_3\text{MgI}$$

$$C_4H_8 + C_4H_{10} \qquad C_3H_7-CH(OH)CH_3$$

(2) $CH_3\cdot + n\text{-}C_4H_9OCH_2-CH_2-C_2H_5 \longrightarrow CH_4 + C_4H_9OCH_2-\underset{\cdot}{CH}-C_2H_5$

$$C_4H_9OCH_2-\underset{\cdot}{CH}-C_2H_5 \longrightarrow n\text{-}C_4H_9O\cdot + CH_2=CH-C_2H_5$$

$$\downarrow \cdot\text{MgI}$$

$$n\text{-}C_4H_9OMgI \longrightarrow n\text{-}C_4H_9OH$$

From the data on the electrolysis of *n*-butyl-, isobutyl-, *tertiary*-butyl- and *n*-hexylmagnesium bromides it follows that *with increasing chain length the tendency of a radical to dimerize increases and its ability to react with the solvent decreases.*

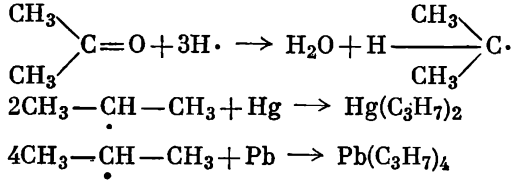
Electrolysis of an aqueous or an alcoholic solution of methylmercuric chloride results in the formation of a black deposit on the cathode, to which the structure of the free radical $CH_3 - Hg\cdot$ with an unsaturated mercury atom is attributed. Methylmercury is also formed upon electrolysis of methylmercuric chloride in liquid ammonia. This substance is a good conductor of electricity. At ordinary temperatures $CH_3Hg\cdot$ decomposes rapidly into mercury and dimethylmercury [72].

Ethylmercury, $C_2H_5Hg\cdot$, may be prepared under similar conditions.

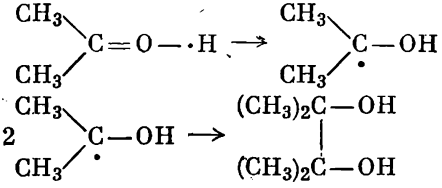
Both substances are perhaps not free radicals, but monovalent mercury compounds of the R — Hg — Hg — R type.

### Cathodic Reduction of Carbonyl Compounds

Electrolytic reduction of ketones and certain aldehydes at lead or mercury cathodes results in good yields of organometallic compounds. For instance, reduction of acetone results in diisopropylmercury and tetraisopropyllead, probably by the following mechanism:

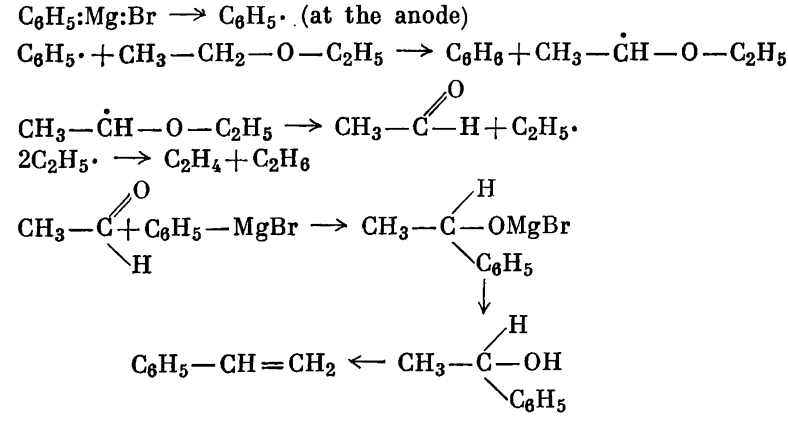


Electrolytic reduction of ketones generally also gives pinacones, and reduction of aldehydes, glycols. These substances are evidently dimers of free radical intermediates formed by the addition of one atom of hydrogen to a carbonyl compound.



### Preparation of Aryl Radicals by Electrolysis

Electrolysis of phenylmagnesium bromide in dry ether yields mainly benzene and styrene, traces of biphenyl, *p*-terphenyl, higher hydrocarbons and a small amount of ethanol.



Electrolysis of benzylmagnesium bromide gives good yields of dibenzyl, because the benzyl radical is more stable and, consequently, does not immediately react with the solvent, but may collide with another benzyl radical.

Investigation of the electrolysis of organomagnesium compounds of the arylmagnesium halide type suggests that free radicals of the phenyl type possess more free energy and are consequently more reactive than free radicals of the ethyl type because it is characteristic of the former (when generated by electrolysis) to react with the solvent, while the latter are more likely to dimerize or disproportionate.

## 5-7.9 Decomposition of Azo- and Diazo Compounds

Many decomposition reactions of azo- and diazo compounds cannot be attributed to ionic mechanisms. These reactions are evidently homolytic, i.e., they proceed through a stage wherein neutral organic radicals are formed.

The most important reactions of this type are described below.

### Decomposition of Arylazotriarylmethanes

Solutions of phenylazotriphenylmethane in petroleum ether, xylene or ethyl benzoate eliminate nitrogen at about 80° and form triphenylmethyl and benzene (but not biphenyl)

$$(C_6H_5)_3C{-}N{=}N{-}C_6H_5 \xrightarrow{R-H} (C_6H_5)_3C\cdot + N_2 + C_6H_6$$

Decomposition of phenylazotriphenylmethane in benzene or chloroform solution results in a theoretical yield of biphenyl or 4-chlorobiphenyl, respectively:

$$(C_6H_5)_3C{-}N{=}N{-}C_6H_5 \longrightarrow (C_6H_5)_3C\cdot + N_2 + \cdot C_6H_5$$
$$C_6H_5\cdot + C_6H_6 \longrightarrow C_6H_5{-}C_6H_5 + \cdot H$$
$$C_6H_5\cdot + C_6H_5Cl \longrightarrow p\text{-}ClC_6H_4 \text{ —} C_6H_5 + \cdot H$$

The reaction of the phenyl radicals with the solvent proceeds so rapidly that dimerization does not take place at all.

The use of (a) toluene, (b) pyridine, and (c) carbon tetrachloride, as solvents, resulted, among other reaction products, in (a) a mixture of methyl biphenyls, (b) a mixture of phenylpyridines, and (c) triphenylchloromethane and chlorobenzene.

### Decomposition of Diazoacetates

Phenyl diazoacetate is a very convenient substance for the preparation of free radicals, because the latter form most readily in decompositions carried out in non-dissociating solvents with low

dielectric constants, and phenyl diazoacetate is quite soluble in most organic solvents.

In 1934 Grieve and Hey [73] showed that phenyl diazoacetate undergoes monomolecular decomposition at a constant rate in a great variety of solvents. The reaction rate is determined by the stage wherein nitrogen is evolved:

$$C_6H_5—N{=}N—OCOCH_3 \longrightarrow C_6H_5^{\cdot} + N_2 + {\cdot}O—CO—CH_3$$

According to these authors, the solvent does not participate in this stage of the reaction. The secondary process is the reaction of free radicals with the solvent:

$$C_6H_5^{\cdot} + C_6H_5—X \longrightarrow C_6H_5—C_6H_4—X + {\cdot}H$$

Since the *para* derivative always forms irrespective of the nature of X, it follows that the phenyl radical is a nonpolar free radical.

Waters [74] showed that aryl radicals obtained from phenyl diazoacetate possess an unusually high reactivity (like Paneth's radicals).

Organic solvents of all types are attacked by the decomposition products of phenyl diazoacetate. Decomposition in *n*-hexane, cyclohexane, ether, dixane, acetone, ethyl acetate, acetonitrile, and acetic anhydride always yields benzene and acetic acid.

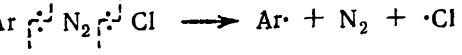
The metals zinc, iron, copper, tin and lead are attacked on decomposition of phenyl diazoacetate even in an excess of caustic soda; this can by no means be attributed to the action of acetic acid in the presence of atmospheric oxygen, and can be due only to the action of the free radical $CH_3COO{\cdot}$. An important proof of the presence of free radicals in this decomposition is the formation of organometallic compounds.

Thus, when phenyl diazoacetate is decomposed in carbon tetrachloride in the presence of mercury, phenylmercuric chloride is formed.

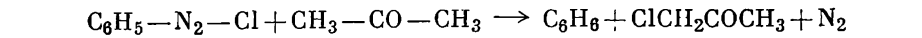
The reaction between phenyl diazoacetate and pyridine results in a mixture of $\alpha$-, $\beta$- and $\gamma$-phenylpyridines, with a total yield of 60 per cent. Only neutral phenyl radicals are capable of reacting with the formation of such reaction products.

### Decomposition of Aryldiazonium Chlorides

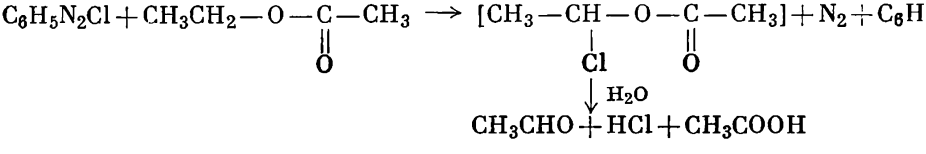
Generally, free radicals do not form in aqueous acid solutions of aromatic diazonium compounds, but they may form in nonaqueous solvents, in which ionic dissociation is less probable. Under these conditions aryldiazonium chlorides, apparently, decompose in the form of a covalent diazo compound:

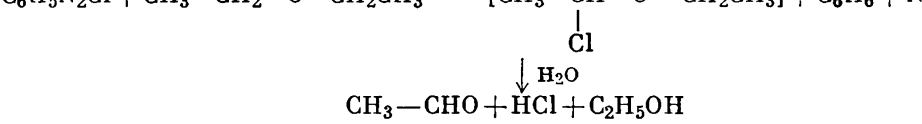


Waters [75] found that free radical decomposition occurs in alcohol, acetone, ethyl acetate, acetonitrile and ether. Some of the reactions studied by Waters were quite unexpected:

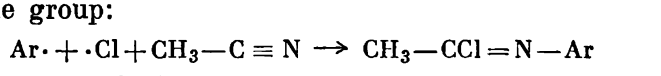


It is clear that in this case it is the Cl· radical and not the inert chloride ion that reacts. Both ethyl acetate and diethyl ether are converted to acetaldehyde; evidently, they are also initially chlorinated.

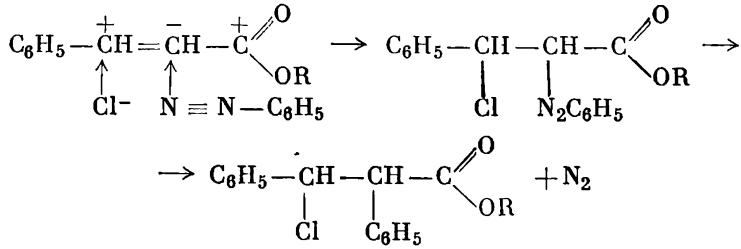




The free radicals formed on decomposition of $ArN_2Cl$ may add to the nitrile group:



Meerwein and coworkers [76] regarded these and other similar reactions as ionic reactions, wherein the direction of addition is determined by the ester, carbonyl or nitrile groups:



However, Koelsch [77] described examples of addition which cannot be explained by Meerwein's polar mechanism*. Thus, in acetone solution containing a little cupric chloride phenyldiazonium chloride reacts with acrylonitrile as follows:

* For reviews of Meerwein's reaction see [78, 79].

The addition of phenyldiazonium chloride to crotonic acid and to esters of cinnamic acid proceeds according to the following scheme:

$$CH_3-CH=CH-COOH + C_6H_5N_2Cl \longrightarrow CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\underset{\displaystyle Cl}{\underset{|}{CH}}-COOH + N_2$$

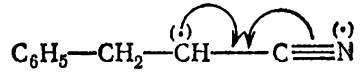
$$C_6H_5-CH=CH-COOC_2H_5 + C_6H_5N_2Cl \longrightarrow C_6H_5-\underset{\displaystyle Cl}{\underset{|}{CH}}-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-COOC_2H_5$$

These inconsistencies with Meerwein's polar mechanism definitely indicate a free radical mechanism.

Addition of a phenyl radical to a molecule of acrylonitrile may result in the intermediate radicals (I) or (II):

$$C_6H_5^{\bullet} + CH_2=CH-C\equiv N \longrightarrow \begin{cases} C_6H_5-CH_2-\dot{C}H-C\equiv N & \text{(I)} \\ \text{or} \\ \dot{C}H_2-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-C\equiv N & \text{(II)} \end{cases}$$

Actually, however, the phenyl radical should add more easily to the methylene group of acrylonitrile, because the radical (I) possesses less energy (is more stable) owing to the conjugation of the unpaired electron with the $\pi$ electrons of the nitrile group.



Radical (II) possesses no such possibilities and the electron is localized on a single carbon atom.

In the case of addition to cinnamic acid, of the two radicals:

$$C_6H_5-\underset{\displaystyle \cdot}{CH}-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-COOC_2H_5 \quad \text{(III)} \qquad \text{and} \qquad C_6H_5-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\underset{\displaystyle \cdot}{CH}-COOC_2H_5 \quad \text{(IV)}$$

the radical (III) is more stable because of the interaction of the odd electron with the $\pi$ electrons of the aromatic ring.

In Koelsch's opinion the role of the copper salt consists in abstraction of one electron from the radical to form a cation which can attract halide anions:

$$CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\underset{\displaystyle \cdot}{CH}-COOH + Cu^{++} \longrightarrow CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\overset{+}{CH}-COOH \xrightarrow{Cl^-}$$

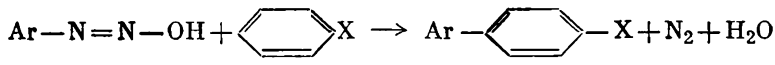
$$\longrightarrow CH_3-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\underset{\displaystyle Cl}{\underset{|}{CH}}-COOH$$

The chlorine atom freed during the initial dissociation of phenyldiazonium chloride oxidizes $Cu^+$ to $Cu^{++}$.

$$Cl^{\cdot} + Cu^+ \rightarrow Cl^- + Cu^{++}$$

Reactions of the type of $ArN_2X \rightarrow ArX + N_2$, which generally require such catalysts as salts of monovalent copper or metallic copper (reactions of Sandmeyer and Gattermann) are apparently not ionic, but radical ones [80].

The decomposition of diazohydrates was studied as early as 1895 by Bamberger. In attempting to develop a convenient method for the synthesis of biphenyl derivatives, Gomberg and coworkers extended Bamberger's investigations and worked out the reaction



which became of great importance to synthesis (Gomberg's reaction).

This reaction is also of a radical nature, because, irrespective of the nature of X, the aryl radical from aryldiazohydrate always enters into the *para*- or *ortho*-position with respect to the substituent already there [81].

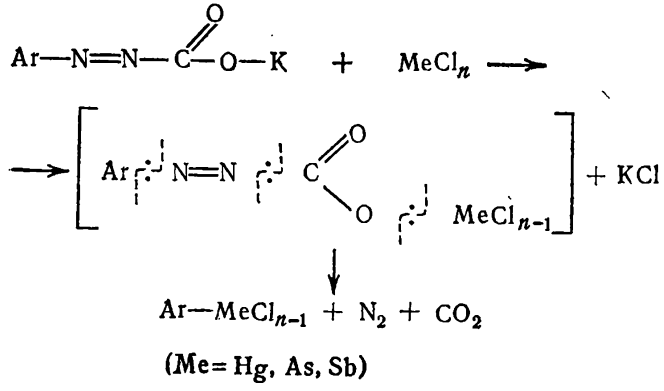
The decomposition of *syn*-diazocyanides in unionized solvents is catalyzed by copper powder and yields free aryl and free cyanide radicals which react with the solvent. The latter is evidence of the incorrectness of Hantzch's views, according to which adjacent radicals immediately unite after the elimination of nitrogen.

### Decomposition of Diazo Compounds and Double Diazonium Salts Resulting in the Formation of Organometallic Compounds

The decomposition of diazo compounds and double diazonium salts to form organometallic compounds has been studied extensively for purely synthetic purposes. The mechanism of these reactions, however, has not been sufficiently investigated. As will be shown in the next section, such reactions may be both homolytic and heterolytic.

Three methods of synthesis of organometallic compounds are similar in the conditions at which they proceed, these conditions generally favouring radical reactions: the methods of Nesmeyanov and Waters, and the method of synthesis through arylazocarboxylic acid salts.

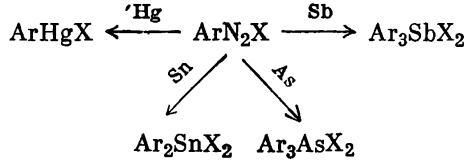
The action of heavy metal chlorides on potassium arylazocarboxylate results in the formation of organometallic compounds:



(Me= Hg, As, Sb)

The reaction is of a radical nature [82].

The method of Waters (1937) consists in reacting aryldiazonium chloride with metallic powders in an organic solvent [83, 84].



Because of low yields this method is of little preparative value.

The most important method of synthesizing organometallic compounds through diazo compounds is the method of double diazonium salts or the diazo method of Nesmeyanov, consisting in decomposing double salts of aryldiazonium halides and heavy metal halides by metallic powders in acetone or ethyl acetate solution.

This method was discovered in 1929 for organomercury compounds [85].

$$ArN_2Cl \cdot HgCl_2 + 2Cu \longrightarrow Ar{-}HgCl + N_2 + CuCl_2$$

In subsequent years the method was extended to the synthesis of organometallic compounds of tin, lead, thallium, bismuth, arsenic and antimony [82, 86].

This reaction generally proceeds according to the following diagram:

$$(ArN_2X)_m \cdot MeX_n + \frac{2m}{p}\,Me' \longrightarrow Ar_mMeX_{n-m} + \frac{m}{p}\,Me'X_p + N_2^*$$

The mechanism of reactions of diazo compounds resulting in the synthesis of organometallic compounds, and in particular, the mechanism of Nesmeyanov's reaction, is not fully elucidated, though numerous investigations have been made in this field.

* Me is the metal being arylated, with a valence of $n$. Me' is the metal reducer with a valence of $p$.

After a thorough investigation of free radical reactions of diazo compounds in organic solvents (aryldiazonium chlorides, diazoacetates), Waters came to the conclusion that Nesmeyanov's reaction is also of a radical, homolytic nature [87].

The main proof of the homolytic nature of Nesmeyanov's reaction is the character of the side reaction which comprises reactions of aryl free radicals with the solvent.

Recently, however, investigations of the mechanism of Nesmeyanov's reaction produced a number of facts which made necessary a critical reappraisal of this point of view [88].

The basic argument in favour of the homolytic nature of Nesmeyanov's reaction is the formation of by-products resulting from reactions of a clearly radical character. However, another explanation of this fact is also possible.

Double diazonium salts are capable of exchange reactions in organic solvents, e.g.:

$$ArN_2Cl \cdot FeCl_3 \xrightarrow{HgCl_2} ArN_2Cl \cdot HgCl_2$$
$$ArN_2Cl \cdot FeCl_3 \xrightarrow{SbCl_3} ArN_2Cl \cdot SbCl_3$$
$$ArN_2Cl \cdot FeCl_3 \xrightarrow{AsCl_3} ArN_2Cl \cdot AsCl_3$$
$$ArN_2Cl \cdot FeCl_3 \xrightarrow{BiCl_3} ArN_2Cl \cdot BiCl_3$$

Most probably, double diazonium salts of ferric chloride are partly dissociated in organic solvents:

$$ArN_2Cl \cdot FeCl_3 \rightleftarrows ArN_2Cl + FeCl_3$$

Addition of a heavy metal salt results in a less soluble salt:

$$ArN_2Cl + MeCl_n \longrightarrow ArN_2Cl + MeCl_n$$

Since double diazonium salts may dissociate to form free diazonium, it is apparent that a certain amount of free aryldiazonium * is always present under the conditions of Nesmeyanov's reaction. Decomposition of $ArN_2Cl$ by a metallic powder (or thermal decomposition) naturally results in the formation of free radicals (and atomic chlorine) which react with the solvent. However, this is a side reaction with respect to the reaction of the double diazonium salt with the metal to form the metalloorganic compound.

A study of the dependence of the rates of the reactions:

$$X-C_6H_4-SbCl_4 \cdot C_6H_5N_2Cl + Fe \longrightarrow X-C_6H_4(C_6H_5)SbCl_3 + N_2 + FeCl_2$$

on the nature of the substituent X led to the assumption that the decomposition of double diazonium salts is heterolytic.

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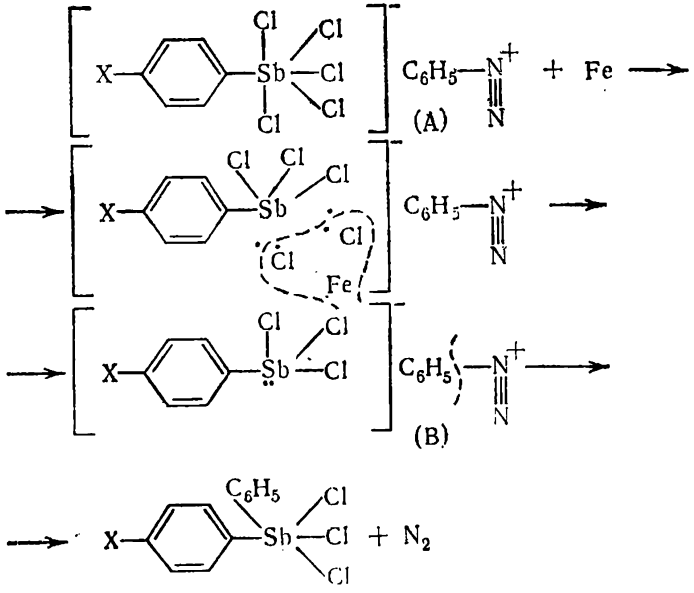
* The ability of double diazonium salts to dissociate in acetone into free aryldiazonium has been confirmed by kinetic investigations [89].

It was shown that the substituents X increase the reaction rate in the sequence of increasing electron-donor properties:

$$O_2N < Cl < H < CH_3 < C_2H_5O$$

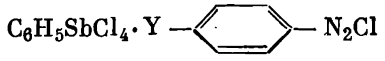
As electron density is not a determining factor in radical reactions (page 282) such a simple dependence of reaction rates on the electronegative properties of the substituents is puzzling if the reaction is considered homolytic.

On the contrary, the observed dependence may be explained by assuming the decomposition of double salts by iron powder to be heterolytic, e.g., to proceed according to the following diagram:




Naturally, decomposition of the intermediate double salt B (addition of an $Ar^+$ cation to the free electron pair of the antimony atom) may be enhanced by substituents of type I and impeded by substituents of type II.

The dependence of the rates of decomposition of double salts




on the nature of the substituent Y is also in accord (see page 384) with the hypothesis of heterolytic mechanism of the reaction in question (rate of reaction decreases with increasing electron-donor properties of the substituents).

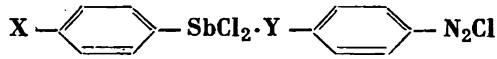
Stability studies of double diazonium salts of the type $ArSbCl_2 \cdot Ar'N_2Cl$, which generally decompose easily in acetone or ethyl acetate according to the equation:

$$ArSbCl_2Ar'N_2Cl \longrightarrow ArAr'SbCl_3 + N_2$$

point to similar conclusions. The stability of salts of the type $ArSbCl_2 \cdot Ar'N_2Cl$ is varied and depends on the nature of Ar and Ar'. Substituents of the first type in the radical of the organoantimony component lower, and in the radical of the diazo component increase, the stability of double salts. Conversely, substituents of the second type in the radical of the organoantimony component increase, and in the radical of the diazo component decrease, the stability of double salts. Many salts (especially those which contain a substituent of the second type in the radical of the diazo component and a substituent of the first type in the radical of the organoantimony component) are not capable of existence and, in all the attempts to prepare them, decompose at once with the formation of diarylantimony trichloride.

TABLE 5-6*

**Stability of the Double Salts**



**Depending on the Nature of X and Y**

| No. | Substituent Y | Substituent X: p-$O_2N$ — | p-$H_2NO_2S$ — | p-H | p-$CH_3$ |
|---|---|---|---|---|---|
| 1. | p-$O_2N$ — | — | — | — | — |
| 2. | m-$O_2N$ — | — | — | — | — |
| 3. | p-$C_2H_5OOC$ — | — | — | — | — |
| 4. | p-$CH_3$—C(=O)— | + | — | — | — |
| 5. | p-H — | + | + | + | — |
| 6. | p-$CH_3$ — | + | | + | + |
| 7. | p-$CH_3O$ — | + | | + | + |
| 8. | p-$C_2H_5O$ — | | + | + | |
| 9. | p-$(CH_3)_2N$ — | + | + | + | + |

* The convention used in the table is as follows:

[+] double salt obtained;

— salt incapable of existence (decomposes);

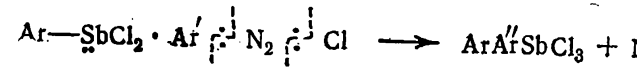
[ ] blank square means that such a salt has not been investigated.

Table 5-6 gives data on the stability of double diazonium salts of arylstibine dichlorides obtained in the reaction:

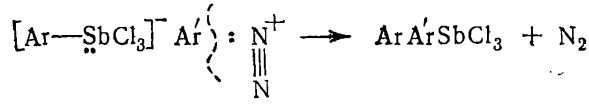
$$ArSbCl_2 + Ar'N_2Cl \cdot FeCl_3 \longrightarrow ArSbCl_2 \cdot Ar'N_2Cl + FeCl_3$$

Of greatest interest is the definite dependence of the stability of these salts on the nature of the radical of the organoantimony part of the double salt.

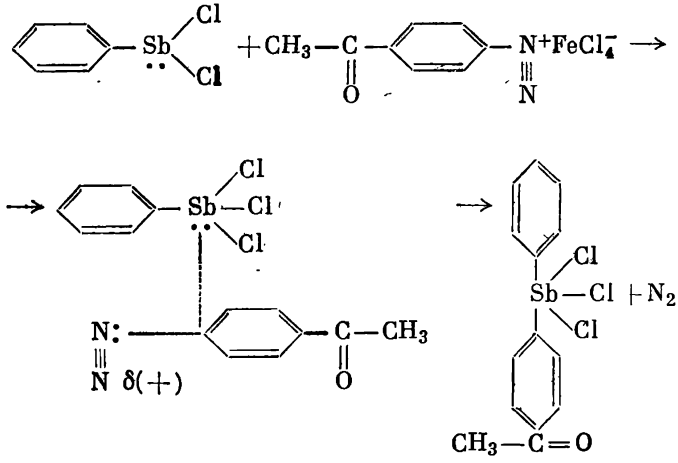
Apparently, this phenomenon cannot be understood if the generally accepted viewpoint that decomposition of double diazonium salts is a radical reaction, is maintained.



If, on the other hand, we assume the mechanism to be heterolytic, the dependence

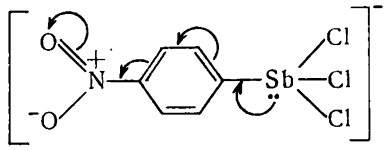


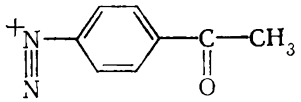
of the stability of $ArSbCl_2 \cdot Ar'N_2Cl$ salts on the nature of Ar can be accounted for. Instability of double diazonium salts with orienting substituents of the second type in the radical of diazo component is evidently a result of the reaction between the anion of the organoantimony compound and the aryldiazonium cation; the latter, in its turn, is a result of the presence, on the one hand, of a free electron pair at the antimony atom, and, on the other, of the presence of a partial positive charge on the carbon atom of the benzene ring linked with the nitrogen owing to drawing away of the electrons by substituents of the second type, e.g.:



Substitution into the *ortho-* or *para*-position of the phenyltrichlorostibine radical of a II type substituent results in attraction of the free electron pair

of the antimony atom in the direction of the benzene ring,



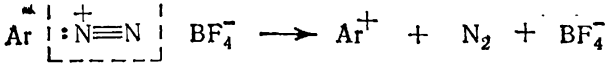


resulting in lowering of the interaction between the antimony atom and the carbon atom of the diazonium radical, and consequently in increased stability of the double salt. This explains the ability of *para*-nitrophenyldichlorostibine to give stable double salts with aryldiazonium halides even when the diazonium radical contains a II type substituent (acetyl) [90].

The above data favour the hypothesis that Nesmeyanov's reaction is heterolytic in nature. * It should, however, be taken into consideration that among the numerous reactions of decomposition of double diazonium salts [91] resulting in organometallic compounds, some may be heterolytic and others homolytic.

### Decomposition of Aryldiazonium Borofluorides

Some of the better established examples of heterolytic reactions of diazo compounds in organic solvents are the processes of decomposition of aryldiazonium borofluorides into aryl cations, investigated by Nesmeyanov and coworkers:



If the aryl radical formed during the decomposition of aryldiazonium chloride enters into the *para*- or *ortho*-position with respect to a substituent of either the I or the II kind in the benzene ring, the aryl cation formed on decomposition of aryldiazonium borofluoride obeys the rules of orientation like any other electrophilic reagent and enters the benzene ring in the *meta*-position if it contains a *meta*-orienting group [92].

* The synthesis of organometallic compounds after Waters (page 381) probably passes through a stage of intermediate formation of double diazonium salts of metal chlorides and is, therefore, a modification of Nesmeyanov's diazo method:

$$n\mathrm{ArN_2Cl} + \mathrm{Me} \longrightarrow n\mathrm{Ar}\cdot + \mathrm{N_2} + \mathrm{MeCl}_n$$

$$\mathrm{ArN_2Cl} + \mathrm{MeCl}_n \longrightarrow \mathrm{ArN_2[MeCl}_{n+1}\mathrm{]} \xrightarrow{\mathrm{Me}} \mathrm{Ar{-}MeCl}_{n-1}$$

If, as has been shown by Koelsch [93], the aryl radical formed on decomposition of $ArN_2Cl$ in the presence of an unsaturated compound adds to the latter contrary to Markovnikov's rule,

$$C_6H_5N_2Cl_2 + CH_3-CH=CH-COOC_2H_5 \longrightarrow CH_3-\underset{C_6H_5}{CH}-\underset{Cl}{CH}-COOC_2H_5 + N_2$$

the phenyl cation formed on decomposition of phenyldiazonium borofluoride adds to unsaturated compounds according to Markovnikov's rule [92] because it is a positively charged particle.

By decomposing phenyldiazonium borofluoride in bromobenzene and in chlorobenzene it was found possible to synthesize diphenylbromonium and diphenylchloronium salts [94]:

$$C_6H_5-N\equiv N^{+}\ BF_4^- + C_6H_5-\ddot{Br}: \longrightarrow \left[C_6H_5-\ddot{\underset{\cdot\cdot}{Br}}-C_6H_5\right]^{+} BF_4^- + N_2$$

$$C_6H_5-N\equiv N^{+}\ BF_4^- + C_6H_5-\ddot{Cl}: \longrightarrow$$

$$\longrightarrow \left[C_6H_5-\ddot{\underset{\cdot\cdot}{Cl}}-C_6H_5\right]^{+} BF_4^{\ominus} + N_2$$

When phenyldiazoacetate which is known to form phenyl free radicals (page 376) is decomposed in bromobenzene and chlorobenzene, bromonium and chloronium compounds do not form. This is clearly due to the fact that an aryl cation can add to the free electron pair of bromine or chlorine in $C_6H_5-\ddot{\underset{\cdot\cdot}{X}}:$, but an aryl radical cannot.

It should be pointed out that the formation of an aryl cation on decomposition of aryldiazonium borofluoride is not surprising because it is accompanied by the formation of an energetically stable $BF_4^-$ anion.

### Decomposition of Diaryl Halogen Salts

There is a considerable similarity between the decomposition of various diazo compounds and iodonium salts by powdered metals.

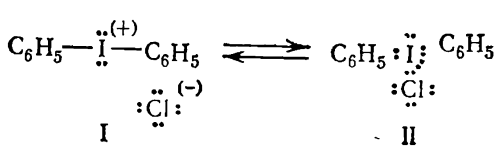
Sandin, McClure and Irwin [95] showed that when diphenyliodonium iodide is refluxed in *n*-propanol in the presence of metallic mercury a certain amount of phenylmercuric iodide results:

$$(C_6H_5)_2II + Hg \longrightarrow C_6H_5HgI + C_6H_5I$$

Under the same conditions diphenyliodonium chloride forms phenylmercuric chloride with a yield of 40%. This reaction proceeds to some extent even in boiling water in the presence of lime.

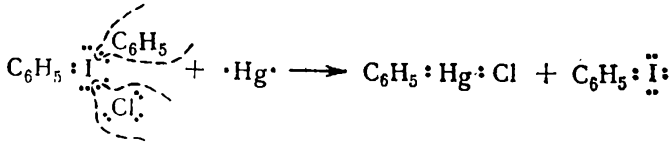
Diphenyl telluride is formed when diphenyliodonium iodide is refluxed in *n*-propanol in the presence of powdered tellurium; diphenyliodonium iodide yields triphenylantimony sulphide when treated with an aqueous solution of sodium sulphide containing powdered antimony.

These reactions are so much like the homolytic reactions of decomposition of aryldiazonium salts by powdered metals that Sandin, McClure and Irwin suggested the hypothesis that an equilibrium is established between iodonium salts and the covalent complex in which the iodine atom possesses more than eight valence electrons (*d*-electrons also participate in the formation of valence bonds):

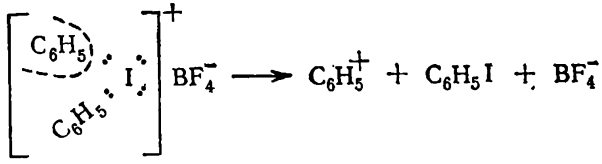


I II

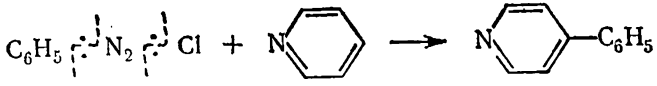
Probably iodonium salts decompose, at least partially, homolytically in the covalent form II, resulting in the formation of aryl free radicals and atomic halogen; the latter yield organometallic compounds by attacking the metal:



It is interesting that phenyl cations and not phenyl radicals are ormed in the decomposition of diphenyliodonium borofluoride:

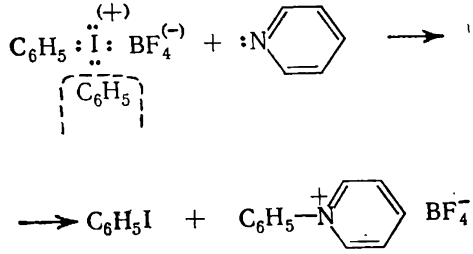


If the phenyl radical formed on decomposition of phenyldiazonium chloride enters the pyridine* nucleus



* A mixture of α-, β- and γ-phenylpyridines is formed.

the phenyl cation formed by the decomposition of diphenyliodonium borofluoride adds to the free electron pair of the nitrogen, as Makarova and Nesmeyanov [96] have shown, giving an 88% yield of phenylpyridinium

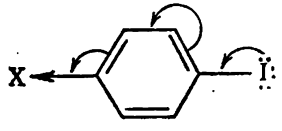


Unlike diphenyliodonium iodide and chloride, diphenyliodonium borofluoride does not form an organomercury compound with metallic mercury.

When a diaryliodonium borofluoride is heated in a solution of aryl iodide labeled with the isotope $^{131}I$, the following isotope exchange reaction occurs [97]:

$$Ar_2I^+BF_4^- + Ar\overset{*}{I} \rightleftarrows Ar_2I^+BF_4^- + ArI$$

In the course of the reaction aryl passes in the form of a cation from the iodine atom of the diaryliodonium borofluoride to the iodine atom of ArI, forming a bond at the unshared electron pair of the latter. The reaction is slowed down when the aryl is a phenyl radical with an electronegative substituent, e.g., $O_2N - C_6H_4$ or $C_2H_5OOCC_6H_4$. This is evidently due to lowering of the electron density at the iodine atom of the ArI molecule because of the electron-withdrawing action of the substituents X.

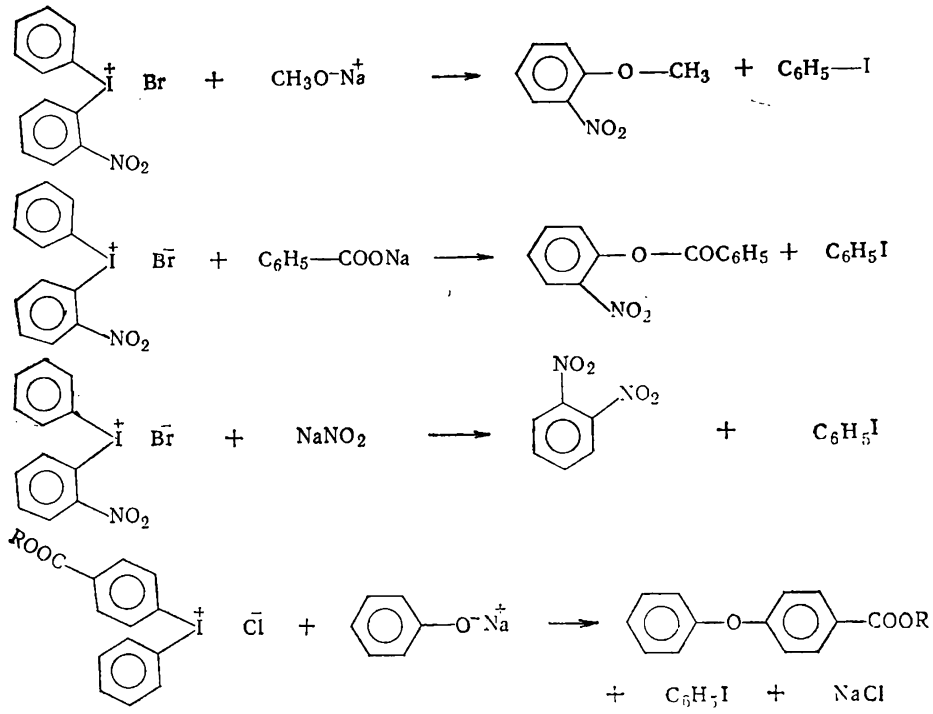


This inhibits the attack of the phenyl cation on the iodine atom. In a study of reactions of mixed diaryliodonium chlorides of the ArAr'ICl type with such nucleophilic reagents as alcoholates and phenolates of alkali metals, Beringer [98] showed that the arylation that occurs in this case is a heterolytic reaction.

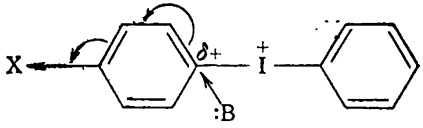
$$Ar_2ICl + R-O-Na \longrightarrow R-O-Ar + ArI + NaCl$$

This conclusion was drawn on the basis that the more electronegative radical from the ArAr'ICl molecule always forms a bond with

oxygen, e.g.:



This phenomenon can easily be understood if it is taken into consideration that under the influence of the electronegative substituent a partial positive charge is formed on the carbon atom linked with iodine, which facilitates nucleophilic attack at this point.



Like aryldiazonium chloride, diaryliodonium chloride forms with metal chlorides double salts of the $Ar_2ICl \cdot nMeCl_n$ type. Methods of synthesizing organometallic compounds of mercury, tin, antimony and bismuth by the decomposition of double salts with metal powders have been devised [99]. For example, organoantimony compounds can be formed by decomposing double salts of diaryliodonium chloride and antimony trichloride in acetone with powdered

antimony.

$$[Ar_2ICl]_2 \cdot SbCl_3 \xrightarrow{Sb} \begin{cases} \rightarrow Ar_2SbCl_3 \\ \rightarrow Ar_3SbCl_2 \end{cases}$$

It was shown that decomposition of double salts of diphenylchloronium chloride and diphenylbromonium chloride with metal chlorides by metal powders results in the formation of organometallic compounds, just as in the case of double salts of diaryliodonium [100]:

$$Ph_2Cl^+HgI_3^- \xrightarrow{Cu} Ph-Hg-I+Ph-Cl+Cu_2I_2$$

$$Ph_2Br^+HgI_3^- \xrightarrow{Cu} Ph-Hg-I+Ph-Br+Cu_2I_2$$

$$(Ph_2Cl^+)_2SnCl_6^{2-} \xrightarrow{Sn} Ph_2SnCl_2$$

$$(Ph_2Br^+)_2SnCl_6^{2-} \xrightarrow{Sn} Ph_2SnCl_2$$

$$Ph_2Cl^+BiCl_4^- \xrightarrow{Bi} Ph_3Bi$$

$$Ph_2Br^+BiCl_4^- \xrightarrow{Bi} Ph_3Bi$$

Organotin compounds are very conveniently synthesized by taking advantage of the reaction of diaryliodonium chloride with stannous chloride [101].

$$2Ar_2ICl+SnCl_2 \rightarrow Ar_2SnCl_2+2ArI$$

The reaction is evidently homolytic. This hypothesis is favoured by the facts that it is catalyzed by the oxygen of the air and that polar factors have no definite pronounced effect on its direction. Thus when unsymmetrical diaryliodonium chlorides ArAr'ICl are decomposed by tin dichloride no predominant bonding with the metal of the more electronegative radical is observed. A mixture of all possible diaryl organotin compounds is formed [102]:

$$ArAr'ICl \xrightarrow{SnCl_2} \begin{cases} \rightarrow Ar_2SnCl_2 \\ \rightarrow ArAr'SnCl_2 \\ \rightarrow Ar'_2SnCl_2 \end{cases}$$

## 5-7.10 Some General Considerations of the Chemistry of Free Radicals in Solution

### Free Radicals in Solution as Kinetically Independent Particles

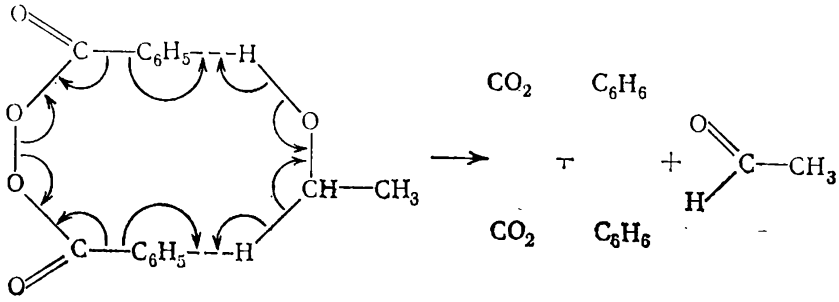
In recent years there has been a tendency to designate all liquid-phase reactions involving homolytic cleavage of covalent bonds as free-radical, though only in a few cases are there sufficient grounds to believe that they pass through a stage of formation of kinetically independent particles.

Because of this it is necessary, in concluding, to consider the possibility of homolytic reactions taking place in solution without the formation of kinetically independent particles (free radicals) through an active-complex stage. The existence of short-lived radicals has been proved directly (by the ESR method) only in a few cases.

So far the chief method of studying reactions of short-lived free radicals in solution is investigation of the end products. The assumption that kinetically independent particles with an unpaired electron form intermediately in solution is a hypothesis in the general case, which has to be proved for each particular instance.

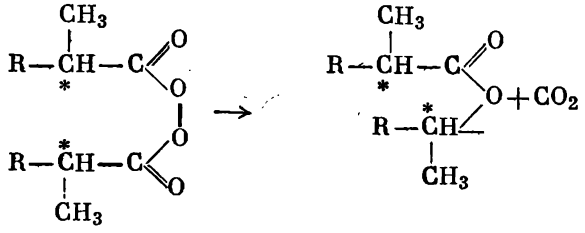
It is equally probable that many reactions, which are anomalous from the point of view of conventional organic chemistry and are ascribed to free radicals, actually pass through an active-complex stage and do not involve the formation of kinetically independent particles.*

Obviously, any so-called free-radical processes can be represented without assuming the intermediate formation of free radicals as taking place within a reaction complex. For example, the decomposition of benzoyl peroxide in ethanol may be represented by the following diagram, each arrow indicating one-electron shift:




* See for example, [96a].

It is very difficult to differentiate between free-radical and homolytic reactions. In some cases stereochemical investigations may offer an important criterion. It has been established [103] that when diaryl peroxides containing an asymmetric carbon atom in the alpha-position decompose, esters are formed in which both asymmetric carbon atoms retain their configuration:



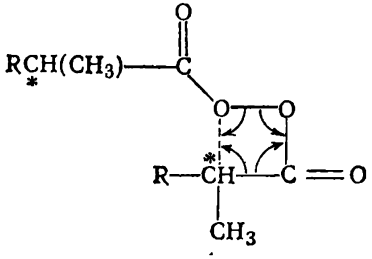
If the reaction passed through the free-radical formation stage

$$[R-\overset{*}{C}H(CH_3)COO]_2 \longrightarrow 2R-\overset{*}{C}H(CH_3)COO\cdot \longrightarrow 2R-CH(CH_3)\cdot + 2CO_2$$

$$R-\overset{*}{C}H(CH_3)COO\cdot + \cdot(CH_3)CHR \longrightarrow R-\overset{*}{C}H(CH_3)-COOCH(CH_3)R$$

the configuration of the asymmetric carbon atom in the alkyl part would not be retained.

It is probable that this homolytic reaction actually does not involve the formation of free radicals and proceeds, for example, through the following cyclic transition stage:



Some other criteria for judging whether radicals are formed as kinetically independent particles during homolytic reactions will be given below.

It would seem that a weighty argument in favour of the initial formation of free radicals are the results of Grieve and Hey's kinetic investigations [73] of the decomposition of phenyldiazoacetate in different solvents.

These authors demonstrated that phenyldiazoacetate undergoes monomolecular decomposition at a constant rate (the evolution of nitrogen was measured) in different solvents (benzene, chloroben-

zene, nitrobenzene, anisole and others), and on the basis of this they came to the conclusion that the initial reaction:

$$C_6H_5—N=N—OCOCH_3 \rightarrow C_6H_5\cdot + N_2 + \cdot OCOCH_3$$

is a process in which the solvent does not participate.

However, this is not the only possible conclusion from these investigations.

In the first place, under the conditions of Grieve and Hey's experiments the possibility of bimolecular reactions following monomolecular reaction kinetics is not excluded, because the excess of solvent, in which the decomposition of phenyldiazoacetate took place was so great that the solvent loss at the end of the reaction averaged only about 1.5 per cent. It is therefore possible that the decomposition of phenyl diazoacetate in organic solvents is actually a bimolecular reaction.

In the second place, although nitrogen was evolved during the decomposition of phenyl diazoacetate at a constant rate in different solvents, the rate is not equal in different cases (though it is of the same order).

These differences in rates possibly indicate that in all the cases studied the elimination of nitrogen is not due simply to the decomposition of the phenyl diazoacetate molecules taking place entirely without the participation of solvents, but may be due to the preliminary formation of some intermediate active complex with the solvent molecules.

Kinetic investigations of the decomposition rates of phenyldiazonium chloride in different alcohols, carried out in great detail by Waring and Abrams [104] showed that although the rate constant of the total reaction

$$k = PZe^{-\frac{E}{RT}}$$

is constant, the energy of activation and the preexponential factor $PZ$ vary in different alcohols. This result also indicates indirectly that an active complex of phenyldiazonium chloride with an alcohol may form first; if this is the case, the activation energy will naturally change when one alcohol is exchanged for another.

Numerous investigations of the rate of decomposition of benzoyl peroxide showed that the decomposition proceeds as a first-order reaction in toluene [105], nitrobenzene [106], benzene [107-109], in mixtures of styrene and benzene [110], vinyl acetate and benzene [109], and in allyl acetate [109].

However, in individual cases it was found that the order of reaction rose as the initial concentration of peroxide was increased. It turned out, further, that the rate of decomposition of benzoyl

peroxide in solvents capable of polymerization is several times that 107, 110] of the decomposition rate in non-polymerizing solvents. Cass [111] showed that the decomposition of benzoyl peroxide in non-polymerizing solvents is not necessarily a first-order reaction. This decomposition may proceed as a bi- and even trimolecular reaction. Consequently, in the case of decomposition of benzoyl peroxide there is no reason to maintain that the initial reaction proceeds without the participation of the solvent.

The formation and reactions of free radicals in solution are naturally more complex than in the gas phase. In solution each particle of the dissolved substance is surrounded by a "cage" of solvent molecules. Therefore decomposition of the molecules of a dissolved substance into free radicals is always more difficult than decomposition of the same substance in the gas phase. Owing to slow diffusion of the radicals formed through the "cage" of solvent molecules the radicals recombine to a large extent.

When the free radicals escape from the "cage", the layer of solvent molecules surrounding each of them inhibits recombination while favouring reaction of the radical with the solvent molecule.

In this connection it would clearly be a major simplification to regard the decomposition of a substance into free radicals in solution as a process entirely independent of the solvent. Rosenthal and Overberger [112] illustrated the mechanism of formation of free radicals and their exit from the "cage" of solvent molecules by the following scheme:

$$\underset{\text{Molecule}}{A{-}B} \xrightarrow{\text{Fast}} \underset{\substack{\text{Two radicals}\\ \text{in the "cage"}}}{[A\cdot\ \cdot B]} \underset{\text{Slow}}{\rightleftharpoons} \underset{\substack{\text{Two radicals}\\ \text{separated by}\\ \text{solvent molecule}}}{[A\cdot]\ [\cdot B]} \xrightarrow[\text{transformation}]{\text{Irreversible}} A\cdot + \cdot B$$

### Transfer Reactions of Identical Radicals in Solution [113]

If a free radical R· is formed in a solvent R — X, from whose molecule it can detach the atom X, the radical may leave the "cage" not only as a result of diffusion but also in a fundamentally different way, viz., by reacting with the molecule of the solvent cage to form an identical radical R·, which is now, however, outside the "cage" of the solvent molecules. A reaction in which this elementary act is repeated many times may be called *relay transfer of radicals*

$$R\cdot + R{-}X \rightarrow R{-}X + R\cdot$$

As a result of relay transfer short-lived radicals R• acquire a longer "group life".[1]

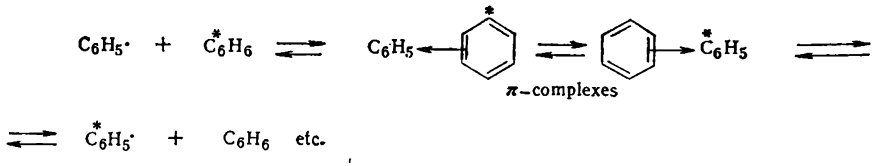
[1] Actually the radicals are not independent of the solvent but form unstable π complexes with the molecules of aromatic solvents; see [113].

The photodecomposition of diphenylmercury in benzene [113] may serve as an example of relay transfer of phenyl radicals.

$$(C_6H_5)_2Hg + C_6H_6 \xrightarrow{h\nu} C_6H_5-C_6H_5 + Hg + C_6H_6$$

If $C^{14}$-labeled benzene is used as the solvent, the resulting diphenyl may contain as much as 14.5% phenyl groups from the solvent.

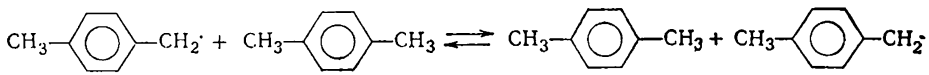
The mechanism of relay transfer of the phenyl radical formed in the reaction under consideration may be imagined as follows*:




The reaction of acyloxy and aryloxy radicals with the corresponding acids [114] may serve as another example of relay transfer of free radicals:

$$R-COO\cdot + R-COOH \rightleftarrows R-COOH + R-COO\cdot$$

An exchange reaction is known to occur between the *p*-methylbenzyl radical and *para* xylene [115].



It should be pointed out, however, that the number of definitely proved cases of relay transfer of radicals is not very large as yet.

### "Frozen" Free Radicals**

The main hurdle in the study of free radicals in the gas, and particularly in the liquid phase is their low concentration. Because of this, proof of the participation of free radicals in liquid-phase reactions could be estalished only in a few cases.

Therefore an important step forward in the study of free radicals was the recent development of a technique of investigating free radicals which consists in their isolation at low temperatures in solids (dies), the molecules of which are not of a radical nature.

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* Recently data were obtained [96a] which indicated that the reaction of relay transfer of phenyl radicals in the cases cited plays no essential part.

** See [117] for review.

he low temperature retards both diffusion (and, therefore, recombiıtion) and the reaction of the radicals with the surrounding olecules.

For example, if the pyrolysis products of toluene vapours are ıpidly cooled to —78° they form a frozen pyrolytic mixture conıining benzyl radicals, which will keep for 1.5 hr [116]. Methods obtaining "frozen" free radicals fall into two groups: condensation om the gas phase together with the matrix molecules (toluene ı the above example) and direct generation of free radicals in the ılid phase, as by the action of light or an ionizing ıdiation.

The preparation of "frozen" radicals and their investigation by ıe electronic spin resonance method will undoubtedly open a new hase in the development of the chemistry of free radicals.

## -7.11 Homolytic Reactions of Organometallic Compounds Initiated by Catalysts

Diphenylmercury is capable of reacting with carbon tetrachloride vhen heated in the presence of benzoyl or acetyl peroxides without rradiation with ultraviolet light. In the presence of acetyl peroxide ıhenylmercuric chloride, benzotrichloride and hexachloroethane re formed. The course of the reaction may be represented by the ollowing diagram:

$$(CH_3COO)_2 \longrightarrow CH_3\cdot + CO_2 + CH_3COO\cdot$$

$$CH_3\cdot + CCl_4 \longrightarrow CH_3Cl + \cdot CCl_3$$

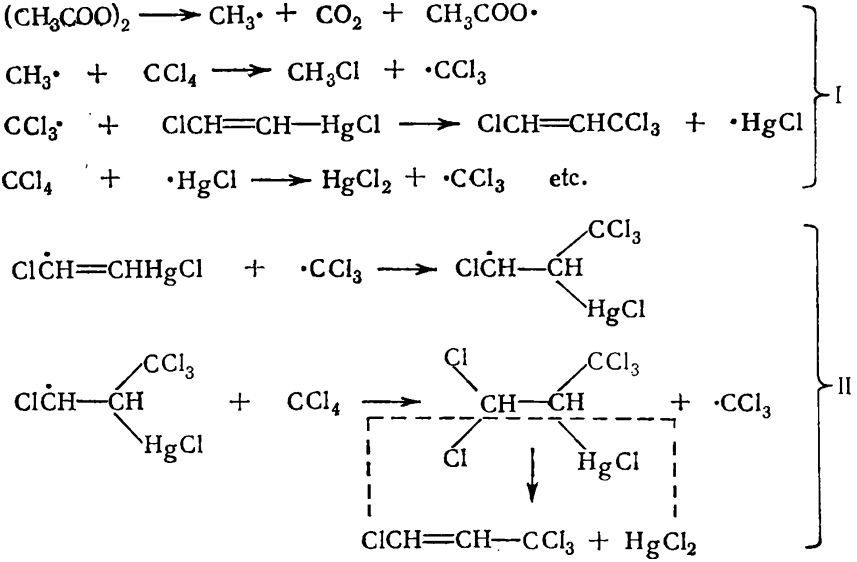
$$CCl_3\cdot + (C_6H_5)_2Hg \longrightarrow C_6H_5-CCl_3 + C_6H_5-Hg.$$

$$C_6H_5-Hg\cdot + CCl_4 \longrightarrow C_6H_5-HgCl + \cdot CCl_3$$

$$2\cdot CCl_3 \longrightarrow CCl_3-CCl_3$$

By using organic peroxides as catalysts Nesmeyanov and Borisov 118] succeeded in accomplishing reactions of *trans*-β-chlorovinylıercuric chloride and *trans-trans*-di-β-chlorovinylmercury with arbon tetrachloride and carbon tetrabromide. Both organomercury ompounds when heated in a sealed tube to 60-70° in the presence f small amounts of benzoyl or acetyl peroxides yield 1,3,3,3-tetrahloropropene-1 and mercuric chloride. Borisov discusses two

possible mechanisms of this reaction:


(CH3COO)2 → CH3· + CO2 + CH3COO·
CH3· + CCl4 → CH3Cl + ·CCl3
CCl3· + ClCH=CH—HgCl → ClCH=CHCCl3 + ·HgCl
CCl4 + ·HgCl → HgCl2 + ·CCl3 etc.
I
ClĊH=CHHgCl + ·CCl3 → ClĊH—CH(CCl3)(HgCl)
ClĊH—CH(CCl3)(HgCl) + CCl4 → CH(Cl)(CCl3)—CH(Cl)(HgCl) + ·CCl3
ClCH=CH—CCl3 + HgCl2
II

The fact that calomel does or does not form as a by-product of the reaction cannot serve as an indication of whether mechanism I or mechanism II is correct, because calomel may form both by dimerization of the radical ·HgCl (mechanism I) and as the result of the reaction

$$HgCl_2 + CCl_3 \rightarrow \cdot HgCl + CCl_4 \text{(mechanism II)}$$

Mechanism I, the mechanism of direct exchange, is confirmed by the fact that the reaction of diphenylmercury with carbon tetrachloride proceeds analogously under the same conditions, benzotrichloride and phenylmercuric chloride being formed. This course of the reaction is difficult to explain by an addition mechanism such as II.

Under similar conditions β-chlorovinylmercuric chloride in benzene solution reacts with carbon tetrabromide in the presence of peroxide yielding 1-chloro-3,3,3-tribromopropene-1.

It is interesting that the photochemical reaction of diphenylmercury with carbon tetrachloride yields different products than the same reaction in the presence of peroxides. In the latter case Borisov found phenylmercuric chloride, benzotrichloride and hexachloroethane among the products. In the case of the photochemical reaction of diphenylmercury with carbon tetrachloride, phenylmercuric chloride and chlorobenzene form and no benzotrichloride is detected. Obviously, the photochemical reaction and the reaction

initiated by peroxides could not have passed through the same intermediate stages. Therefore, it is conceivable that at least one of the reactions in question does not go through the stage of formation of kinetically independent free radicals, but proceeds homolytically within a reaction complex.*

Reactions of some organometallic substances are capable of proceeding homolytically when certain metal halides are added.

Among these are reactions of organomagnesium compounds with carbonyl compounds [119], acid halides [120], and halogen derivatives of hydrocarbons [121] taking place in the presence of cobaltous chloride:

$$R-MgBr + R'-\underset{\underset{O}{\|}}{C}-R'' \xrightarrow{CoCl_2} R'R''C(OH)-CR'R''(OH)$$

$$R-MgBr + Cl-\underset{\underset{O}{\|}}{C}-R' \xrightarrow{CoCl_2} R'-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-R'$$

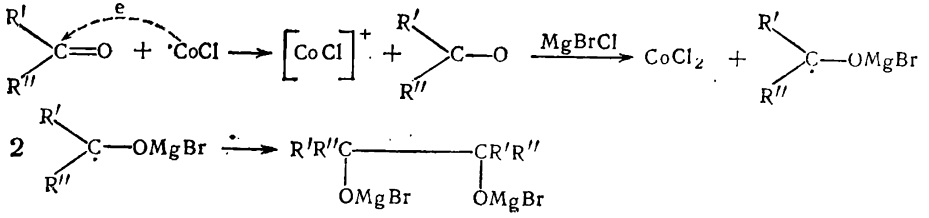
$$Ar-MgBr + Ar'Br \xrightarrow[\text{In the cold}]{CoCl_2} Ar-Ar$$

Kharasch thought that unstable, readily decomposing organocobalt compounds are formed initially:

$$RMgBr + CoCl_2 \rightleftharpoons RCoCl + MgClBr \qquad (a)$$

$$R:CoCl \longrightarrow R\cdot + \cdot CoCl \qquad (b)$$

The reaction with ketones proceeds further as follows:



* In general it should be remembered that the reactivity of free radicals depends on the temperature (for instance, alkyl radicals react with benzene only at temperatures above 300°). However, the difference in the temperatures of photochemical decomposition of diphenylmercury in carbon tetrachloride and its decomposition under the influence of peroxides is so insignificant that it could not be responsible for the difference in reactivity of the phenyl radicals if they existed in both cases as kinetically independent particles.

The reaction with acid chlorides follows the mechanism:

$$R'-\underset{\underset{O}{\|}}{C}-Cl + {}^{\bullet}CoCl \longrightarrow R'-\underset{\underset{O}{\|}}{C} + CoCl_2$$

$$2R'-\underset{\underset{O}{\|}}{C}{}^{\bullet} \longrightarrow R'-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-R'$$

Biaryls form in the reaction with aryl halides* as a result of the reaction between two molecules of the organocobalt compound:

$$2ArCoCl \longrightarrow Ar-Ar + 2{\cdot}CoCl$$

Of all the alkaline metals lithium possesses the highest ionization potential (0.34 eV). Therefore, probably organometallic and particularly aromatic lithium compounds should be largely covalent compounds. The properties of these compounds confirm this assumption.

It is therefore not surprising that the addition of small amounts of cobaltous chloride in the reaction between phenyllithium and butyl bromide causes changes [123] similar to those which take place in case of organomagnesium compounds. Thus, the main products of this reaction in the absence of cobaltous chloride and in its presence (% in parentheses) are as follows: butylbenzene 55% (5%), diphenyl 4% (67%), butane and butylene 0% (8%), octane 0% (20%).

For the reactions of organolithium compounds in the presence of cobaltous chloride the same mechanism has been proposed as for organomagnesium compounds.

### Different Reactivities of Like Radicals

In an investigation of the decomposition of different organometallic compounds during their reactions with metallic chlorides, Woods showed [124] that one and the same radical may behave differently depending on the source of its formation.

Thus, the reaction of methylmagnesium iodide and dimethylmagnesium with zirconium chloride produces methane, this evidently being a result of methyl reacting with the solvent. Methane results also as the sole gaseous product in the reactions of methylmagnesium chloride with thallium trichloride and of dimethylmagnesium with chromous chloride.

However, when silver bromide or iodide react with dimethylmagnesium, pure ethane is formed, and when methyllithium reacts with auric bromide the resulting mixture of gases contains 76.8% ethane and 18.4% methane.

* See [122] for details on the mechanism of the reaction with halogen derivatives.

Thus, the behaviour of the methyl radical depends on the nature of its formation: in some cases it reacts with the solvent, in others it dimerizes, and in still others both processes take place.

Investigation of the decomposition of organosilver compounds $R-Ag \rightarrow R\cdot + \cdot Ag$ taking place at temperatures well below 0° in the case of alkyl compounds and at —18° in the case of aromatics, showed that the radicals do not react with the solvent molecules. If a mixture of organosilver compounds RAg and R'Ag is decomposed in solution, all the possible compounds RR, RR', and R'R' result invariably.

It follows from these facts that decomposition occurs only when the molecules of the organosilver compound react with each other, and all the radical shifts take place within the reaction complex.

Differences are known to exist between the behaviour of aromatic radicals formed by the photolysis of organometallic compounds on the one hand, and by thermal decomposition of peroxides, on the other.

For instance, the α-naphthyl radical formed on photolysis of dinaphthylmercury in carbon tetrachloride does not react with the solvent, while the α-naphthyl radical obtained by thermal decomposition of α-naphthoyl peroxide in carbon tetrachloride reacts with the latter yielding α-chloronaphthalene and hexachloroethane.

The phenyl radical formed in the photolysis of diphenylmercury also behaves differently from the same radical obtained by the decomposition of diphenylmercury in the presence of peroxides (page 398).

Similarly, the behaviour of aryl radicals from organomagnesium compounds in Kharasch's reactions with halogen derivatives of hydrocarbons, differs sharply from the behaviour of the aryl radicals formed, for example, by the decomposition of aryldiazoacetates in the experiments conducted by Grieve and Hey. In the first case the aryl radicals only dimerize; in the second, they react only with the solvent.

If hydrocarbon radicals existed as kinetically independent particles in all the cases considered, there could be no such difference in chemical behaviour because radicals must have a definite chemical structure and, therefore, definite chemical properties. Apparently the different behaviour of the same hydrocarbon radicals is due to the fact that they form as kinetically independent particles (free radicals) in some cases, and change within a reaction complex in others.

"Pure dimerization" proceeding without any side reactions may be regarded to a certain extent as an indicator of the reaction proceeding through the stage of formation of an active complex.

From this point of view it may be assumed that the organometallic compounds of zirconium, thallium and chromium in Wood's experiments react through a stage of formation of free radicals, while

the relatively more thermally stable aromatic cobalt compounds in Kharasch's experiments and the organometallic compounds of silver and gold in Wood's experiments react without forming kinetically independent particles through a stage of active-complex formation.

It should be kept in mind, however, that whereas "pure dimerization" may serve as a criterion of the reaction passing through an active-complex stage, the formation of products of reaction with the solvent does not yet, in the general case, confirm the free-radical nature of the reaction. It is equally probable that this reaction passes through an active-complex stage (page 392).

Thus, a reaction proceeding through an active-complex stage may be monomolecular, bimolecular, etc., and may result in dimerization products of the radicals (even in the case of aromatic radicals) and/or in the products of reaction with the solvent. Reactions which yield reaction products of the radicals with the solvent and no dimerization products in the case of aromatic radicals may pass through the stage of formation of kinetically independent free radicals.

### Carbenes

Carbenes are biradicals possessing a bivalent carbon atom $R_1R_2C:$. The simplest carbene is free methylene, formed on photochemical decomposition [126] of diazomethane* or ketene, or when these substances are decomposed catalytically, as, for example, in the presence of boron compounds [127].

$$H_2C: \vdots \overset{+}{N}::\overset{-}{N}: \xrightarrow{h\nu} H_2C: + N_2; \qquad H_2C: \vdots :CO \xrightarrow{h\nu} H_2C: + CO$$

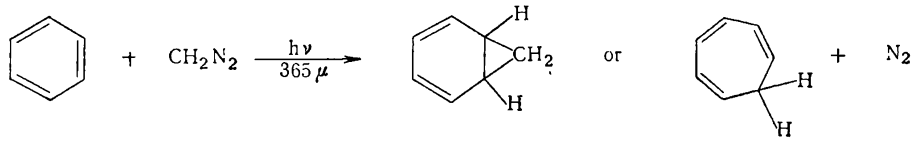
Its half-life is about twice as long as that of a free methyl. In the ground state of methylene the two electrons of its free electron pair evidently have antiparallel spins

$$H_2C: (\downarrow\uparrow)$$

* It is interesting to note that Schmitz and coworkers [125] succeeded recently in synthesizing cyclodiazomethane, an isomer of diazomethane:

$$\begin{matrix} CH_2O \\ NH_3 \\ CH_2O \end{matrix} \longrightarrow H_2C\begin{matrix} NH \\ \diagup\diagdown \\ NH \end{matrix} \xrightarrow{O} H_2C\begin{matrix} N \\ \diagup\diagdown \\ N \end{matrix}.$$

Methylene formed by photochemical decomposition of diazomethane is capable of adding to benzene to form cycloheptatriene [128].



In the reaction with carbon tetrachloride and bromotrichloromethane, methylene enters at the carbon-halogen bond [129-131].

$$CCl_4 + 4CH_2N_2 \xrightarrow{h\nu} ClCH_2-\underset{\displaystyle CH_2Cl}{\overset{\displaystyle CH_2Cl}{\overset{|}{\underset{|}{C}}}}-CH_2Cl + 4N_2$$

$$BrCCl_3 + 4CH_2N_2 \xrightarrow{h\nu} ClCH_2-\underset{\displaystyle CH_2Cl}{\overset{\displaystyle CH_2Br}{\overset{|}{\underset{|}{C}}}}-CH_2Cl + 4N_2$$

**Reactions of Carbenes with Halides.** Diazomethane reacts with mercuric chloride, mercuric iodide [132] and mercuric bromide [133] in such a way that the methylene enters between mercury and the halogen forming a halomethylmercuric halide:

$$CH_2N_2 + X-HgX \longrightarrow X-CH_2-HgX + N_2$$

Diphenyldiazomethane reacts with mercuric chloride in a similar manner:

$$Ph_2CN_2 + Cl-HgCl \longrightarrow Ph_2\overset{\displaystyle Cl}{\overset{/}{C}}-HgCl + N_2$$

In an excess of diazomethane, dihalomethylmercury results:

$$2CH_2N_2 + X-Hg-X \longrightarrow X-CH_2-Hg-CH_2-X + 2N_2$$

The reaction between diazomethane and organomercuric salts $R-Hg-Cl$ results in two symmetric organomercuric compounds:

$$2R-Hg-Cl + 2CH_2N_2 \longrightarrow R_2Hg + (Cl-CH_2)_2Hg + 2N_2$$

Apparently, unsymmetrical organomercuric compounds are formed to begin with

$$R-Hg-Cl + CH_2N_2 \longrightarrow R-Hg-CH_2-Cl + N_2$$

and these are rapidly disproportionated:

$$2R-Hg-CH_2-Cl \longrightarrow R_2Hg + (ClCH_2)_2Hg$$

It is quite probable that the reaction of hydrazones of aldehydes and ketones, resulting in the formation [134] of

$$RR'C{=}N{-}NH_2 + 3Hg(CH_3COO)_2 \xrightarrow{C_6H_6} \rightarrow RR'C\begin{matrix}\diagup HgOCOCH_3 \\ \diagdown OCOCH_3\end{matrix} + 2CH_3COOH + N_2 + Hg_2(OCOCH_3)_2$$

proceeds through a stage of formation of aliphatic diazo compounds; the latter decompose into carbenes RR'C:, which react with mercuric acetate:

$$RR'CN_2 \rightarrow RR'C: \xrightarrow{Hg(OCOCH_3)_2} Hg\begin{matrix}\diagup OCOCH_3 \\ \diagdown CRR' \\ \diagdown OCOCH_3\end{matrix}$$

The reaction with diazomethane is utilized for obtaining organic compounds of Group V elements [135].

Aliphatic diazo compounds react easily at 0-5° with arsenic trichloride, antimony trichloride, bismuth trichloride, yielding generally a mixture of mono-, di- and trialkyl derivatives, depending on the proportions of initial reagents

$$RCHN_2 + EX_3 \rightarrow RCHX{-}EX_2 + N_2$$
$$RCHN_2 + RCHX{-}EX_2 \rightarrow (R{-}CHX)_2EX + N_2$$
$$RCHN_2 + (RCHX)_2EX \rightarrow (R{-}CHX)_3E + N_2$$

Diazoaliphatic compounds react with phosphorus trichloride or tribromide in an analogous manner:

$$R{-}CHN_2 + PX_3 \rightarrow R{-}CHX{-}PX_2 + N_2$$

Pentavalent phosphorus halides of the $POX_3$ type do not react with aliphatic diazo compounds. Phosphorus pentachloride, however, easily forms di- and tri-(ω-haloalkyl) derivatives of pentavalent phosphorus.

Halides of Group IV elements (tin, lead, and silicon) also react with aliphatic diazo compounds, forming the corresponding α-haloalkyl derivatives [136]:

$$R{-}CHN_2 + EX_4 \rightarrow R{-}CHX{-}EX_3 + N_2$$
$$R{-}CHN_2 + RCHX{-}EX_3 \rightarrow (R{-}CHX)_2EX_2 + N_2$$
$$R{-}CHN_2 + (RCHX)_2EX_2 \rightarrow (R{-}CHX)_3EX + N_2$$
$$R{-}CHN_2 + (RCHX)_3EX \rightarrow (R{-}CHX)_4E + N_2$$

At 0-5° tin tetrachloride and tetrabromide react easily with aliphatic diazo compounds in benzene forming all the possible α-haloalkyl tin derivatives. Tin tetrafluoride does not react with diazoaliphatic compounds.

Unlike tin halides, lead chloride does not react with aliphatic diazo compounds, probably because of its practical insolubility in the solvents commonly used for the reaction. Lead tetraacetate reacts with diazomethane according to the equation:

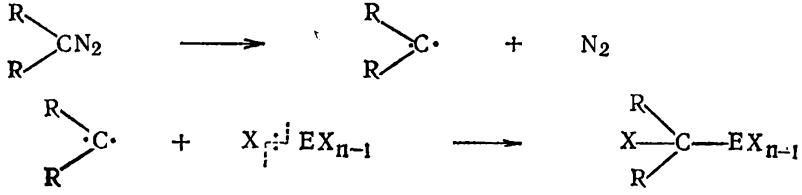
$$CH_2N_2 + Pb(OCOCH_3)_4 \rightarrow CH_2(OCOCH_3)_2 + N_2 + Pb(CH_3COO)_2$$

Chloromethylation of the lead-halogen bond takes place only under specific conditions in the reaction of diazomethane with triethyllead chloride and diethyllead dichloride in the presence of bronze as a catalyst. In the absence of the latter the reaction does not take place even if the mixture is heated.

Haloalkylsilicon halides are prepared from aliphatic diazo compounds and silicon tetrachloride or tetrabromide at —45° to —55°; the reaction is accelerated by bronze or anhydrous copper sulphate.

No organosilicon compounds result from the reaction between silicon tetrafluoride and diazomethane. Only α-chloroalkyl thallium derivatives have been prepared from aliphatic diazo compounds and organic compounds of Group III elements.

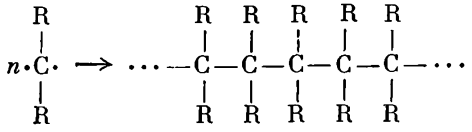
Experimental data on the reactions of aliphatic diazo compounds with the halides of different elements indicate that the reaction is homolytic. It is probable that decomposition of higher aliphatic diazo compounds generally results in alkene biradicals. In reactions of diazo compounds with halides of different elements, the alkenes formed at the instant of the reaction enter at the E — X bonds resulting in the formation of new carbon-element bonds:



The inability of fluorides (for example, tin and silicon tetrafluorides) to react with diazo compounds to form organoelementary compounds is quite possibly due to the fact that homolytic cleavage of the fluorine-element bond requires the expenditure of considerable energy:

The biradical mechanism of the reaction of aliphatic diazo compounds with halides is evidenced by the nature of the side reactions. Thus, in the reaction of aliphatic diazo compounds with silicon tetrachloride or tetrabromide, besides organosilicon compounds, high-molecular-weight hydrocarbons (polyalkenes) are generally formed. The reaction of silicon tetrafluoride with diazomethane results in the formation of polymethylene only. The latter is the only product of the reaction between diazomethane and boron trifluoride.

Polyalkenes form evidently as a result of the polymerization of alkene biradicals:



Such polymerization of alkene biradicals is analogous to dimerization of alkyl free radicals:

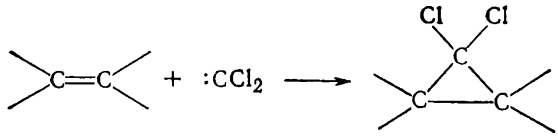
$$R{-}CH_2^{\bullet} + {}^{\bullet}CH_2{-}R \longrightarrow R{-}CH_2{-}CH_2{-}R$$

The radical character of the reactions of aliphatic diazo compounds with the halides of various elements is confirmed by the fact that bronze, which is the usual catalyst for many reactions following the free-radical mechanism, is also a catalyst for the reactions of $RCHN_2$ with $R_3PbX$, $R_2PbX_2$, $SiX_4$, $RSiX_3$ and $R_2SiX_2$.

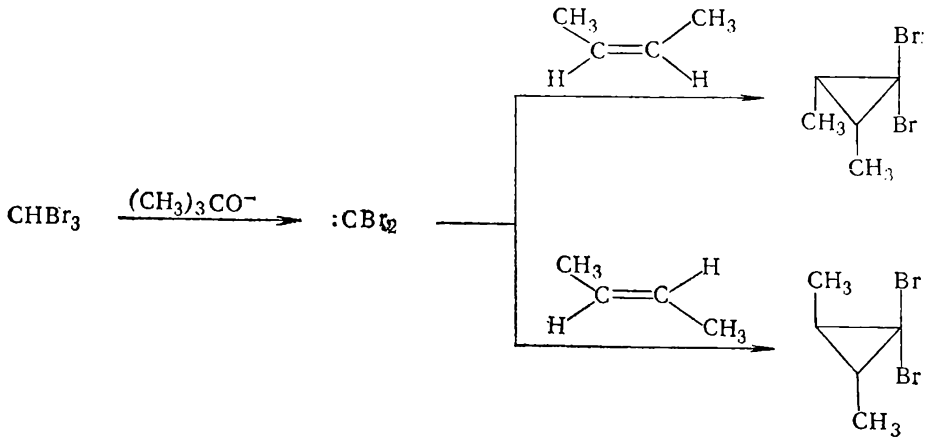
**Halocarbenes.** Recently, due to Doering [137], it has become possible to obtain dihalocarbenes from haloforms and potassium *t*-butylate as unstable intermediates, and to utilize them in synthesis.

$$HCX_3 \underset{\text{Fast}}{\overset{(CH_3)CO-K^+}{\rightleftharpoons}} :CX_3 \underset{\text{Slow}}{\overset{-X-}{\rightleftharpoons}} :CX_2$$

Dichloromethylene, for example, adds to alkenes (cyclohexenes, hexene-1, isobutylene, etc.) at the double bond with the formation of cyclopropane derivatives:




The addition of dibromocarbene to the double bond takes place stereospecifically. For instance, the reaction of $CBr_2$ with *cis*-butene-2 results in *cis*-dimethylcyclopropane; from *trans*-butene-2, dibromo-*trans*-dimethylcyclopropane is formed [138]:

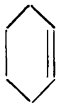


It has been found that addition reactions of dibromocarbene to alkenes feature the same dependence of reactivity of alkenes on their structure, as the heterolytic addition of hydrogen bromide [139] and the oxidation of alkenes by peracids (according to Prilezhayev) [140]. In all three reactions alkenes form the same series of diminishing reactivity:

$$(CH_3)_2C=C(CH_3)_2 > (CH_3)_2C=CHCH_3 > (CH_3)_2C=CH_2 >$$

$$>$$

$$> CH_2=CH-CH=CH_2 >$$



$$> C_6H_5-CH=CH_2 > C_6H_5-CH_2-CH=CH_2$$

It should be pointed out that in free-radical reactions, e.g., in the reactions of addition of $CCl_3Br$ to alkenes in the presence of peroxides, the same compounds form a different sequence. Dichlorocarbene and dibromocarbene, as well as chlorocarbene and bromocarbene, are capable of adding at metal-halogen bonds to form trihalo- and dihalomethyl organometallic compounds, e.g. [141], [142]*.

$$X-Hg-X + :CX_2 \longrightarrow X-Hg-CX_3$$

$$X-Hg-X + :CHX \longrightarrow X-Hg-CHX_2$$

$$R-Hg-X + :CX_2 \longrightarrow R-Hg-CX_3$$

$$R-Hg-X + :CHX \longrightarrow R-Hg-CHX_2$$

Nenitzescu and coworkers obtained dihalocarbenes by the action of silver cation on chloroform, bromoform and trichloroacetic acid [143]

$$CHCl_3 + AgNO_3 \longrightarrow :CCl_2 + AgCl + HNO_3$$

$$CHBr_3 + AgNO_3 \longrightarrow :CBr_2 + AgBr + HNO_3$$

$$CCl_3-COOH + AgNO_3 \longrightarrow :CCl_2 + CO_2 + AgCl + HNO_3$$

and by the thermal decomposition of silver trichloroacetate [144].

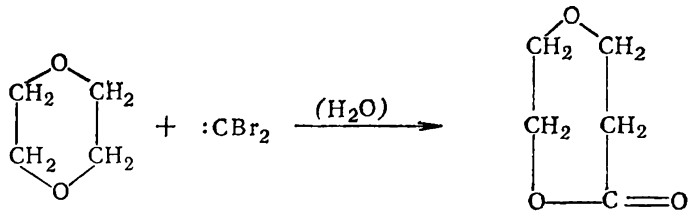
$$Cl_3C-COOAg \longrightarrow :CCl_2 + CO_2 + AgCl$$

Dichlorocarbene is also formed on decomposition of sodium, potassium or ammonium trichloroacetates.

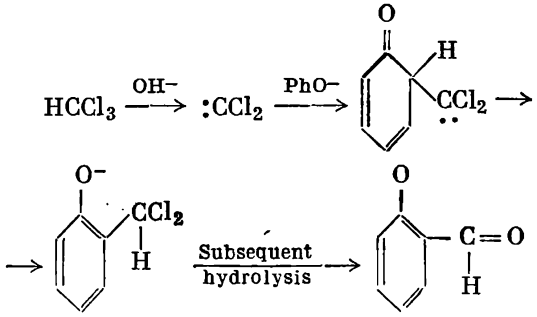
While carrying out the reaction between bromoform and silver nitrate in aqueous dioxane, Nenitzescu established that γ-oxa-ε-lactone is formed, which indicates definitely that dihalocarbenes

* Concerning the possibility of an ionic mechanism of this reaction see [146].

can be introduced at the carbon-oxygen bond [144].



The chemistry of carbenes is now developing rapidly [145]. In this connection the mechanism of some well-known reactions have had to be reconsidered. Thus, it is now clear that the Reimer-Tiemann reaction passes through a stage of formation of dichlorocarbene:



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# 6

# ESTERIFICATION AND HYDROLYSIS

## 6-1 MECHANISM OF ESTERIFICATION REACTIONS

The reaction of an acid with an alcohol resulting in an ester is called *esterification.* This process is reversible, the reverse reaction being called *hydrolysis* or *saponification.*

$$R-COOH+R'OH \underset{\text{Hydrolysis}}{\overset{\text{Esterification}}{\rightleftharpoons}} R-COOR'+H_2O$$

Both reactions are accelerated catalytically by hydrogen ions; hydrolysis is accelerated also by hydroxyl ions.

Esterification is the most thoroughly investigated example of the application of the law of mass action to homogeneous liquid systems. Its study began as far back as 1862-63 by Berthelot and Gilles.

The general equation of the equilibrium of an esterification-hydrolysis reaction is:

$$(p-x)(q-x)=Kx^2$$

where $p$ and $q$ are the molar concentrations of alcohol and acid at the beginning of the reaction; $x$ is molar concentration of ester (and water) at equilibrium; $K$ is equilibrium constant.

If $p$, $q$ and $K$ are known from experiment, $x$ may be calculated.

Table 6-1 lists the results of investigations of the reaction of different amounts of ethanol with 1 mole of acetic acid and the molar concentrations of ester calculated by van't Hoff using the above equation. The table shows good agreement between experimental and calculated data.

The table shows that the quantity of ester increases with increasing concentration of alcohol. The equimolecular ratios of alcohol to acid $x$ is called the *limit of esterification* and equals approximately 2/3. If 8 equivalents of alcohol are mixed with one equivalent of acid, almost all the acid is converted into ester.

It is clear that for complete conversion of alcohol into ester a liarge excess of acid must be used. Conversely, if it is necessary to convert all the acid to ester a large excess of alcohol must be used.

Temperature has a great influence on the speed at which the limit of esterification is reached. Thus, the reaction of equimolecular quantities of ethanol and acetic acid results in 55 per cent ester in 368 days at room temperature, 55.7 per cent in 32 hours at 100° and 66 per cent ester in 24 hours at 150°.

Menshutkin [1] carried out numerous investigations of the esterification reaction and showed that its limit depends on the structure of the alcohol and (to a smaller extent) on the structure of the acid.

TABLE 6-1

**Experimental and Calculated Molar Concentrations of Ester Formed at Different Initial Alcohol Concentrations**

| Molar concentration of alcohol $p$ | Molar concentration of ester $x$ | | Molar concentration of alcohol $p$ | Molar concentration of ester $x$ | |
|---|---|---|---|---|---|
| | Found | Calculated | | Found | Calculated |
| 0.05 | 0.05 | 0.049 | 0.67 | 0.519 | 0.528 |
| 0.08 | 0.078 | 0.078 | 1.0 | 0.665 | 0.667 |
| 0.18 | 0.171 | 0.171 | 1.5 | 0.819 | 0.785 |
| 0.33 | 0.293 | 0.311 | 2.0 | 0.858 | 0.845 |
| 0.50 | 0.414 | 0.423 | 8.0 | 0.966 | 0.945 |

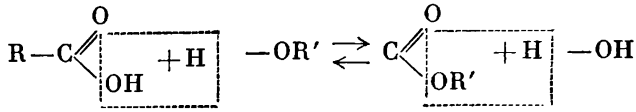
The influence of the structure of the alcohol on the limit of esterification is shown in Table 6-2.

TABLE 6-2

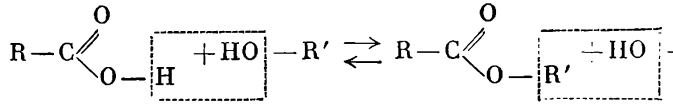
**Dependence of Limit of Esterification on Structure of Alcohol**

| Alcohols | Limit of esterification in per cent (reaction with $CH_3COOH$) |
|---|---|
| *Primary Alcohols* | |
| Methanol | 66.59 |
| Ethanol | 66.59 |
| Propanol | 66.85 |
| Allyl alcohol | 59.41 |
| Benzyl alcohol | 60.75 |
| *Secondary Alcohols* | |
| Isopropanol | 60.52 |
| *sec*-Butanol | 59.28 |
| Diethylcarbinol | 58.66 |
| *Tertiary Alcohols* | |
| Trimethylcarbinol | 6.59 |
| Ethyldimethylcarbinol | 2.53 |

Two mechanisms are possible for the esterification-hydrolysis reaction:



(I)

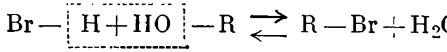


(II)

According to mechanism I the bond between the acyl and the hydroxyl is severed in the acid molecule, and the bond between hydrogen and oxygen in the alcohol molecule is broken; according to mechanism II the bond between the hydrogen and the oxygen in the acid is ruptured, while in the alcohol molecule the break occurs between the alkyl and the hydroxyl.

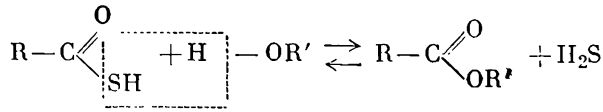
It is very difficult to make a choice between these two mechanisms on the basis of theoretical hypotheses or analogies, because instances are known where the alcohol or acid behaves according to each of the above mentioned mechanisms.

For example, alcohols react with hydrogen halides according to the only possible mechanism, that depicted by II.

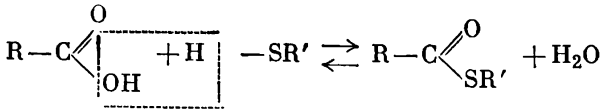


On the other hand, in a number of esterification reactions the RO—H bond is broken according to mechanism I:

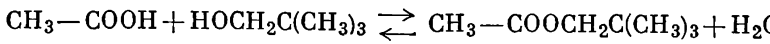
(a) in the reactions of thioacids with alcohols hydrogen sulphide is formed instead of water



but the reaction of carboxylic acids with mercaptans gives $H_2O$ and not $H_2S$



(b) in the preparation of neopentyl acetate by esterification and in its hydrolysis no by-products resulting from rearrangement are found



If free carbonium ion $(CH_3)_3C\overset{+}{C}H_2$ formed, rearranged products would appear in the reaction mixture (pages 550-570).

(c) In the case of alcohols with acyl halides the reaction proceeds according to mechanism I

$$R-\underset{\underset{O}{\|}}{C}-\boxed{Cl+H}-OR' \longrightarrow R-\underset{\underset{O}{\|}}{C}-OR' + HCl$$

An isotope procedure was used to determine the validity of mechanisms I and II.

Esterification of benzoic acid by methanol with an increased heavy oxygen content results in an ester containing heavy oxygen; water contains only ordinary oxygen [2]

$$C_6H_5-C\begin{matrix}O\\ \boxed{OH+H}\end{matrix}-\overset{18}{O}-CH_3 \rightleftarrows C_6H_5-C\begin{matrix}O\\ \overset{18}{O}-CH_3\end{matrix} + H_2O$$

It is clear that esterification proceeds according to mechanism I*.

Hydrolysis follows the same mechanism.

For instance, alkaline hydrolysis of amyl acetate in water containing $O^{18}$ results in amyl alcohol with ordinary oxygen [4].

$$CH_3-COOC_5H_{11}+H_2\overset{18}{O}+NaOH \longrightarrow CH_3-C\overset{18}{O}ONa+C_5H_{11}OH+H_2O$$

On acid hydrolysis of monomethyl succinate with water, enriched in heavy oxygen, all the $O^{18}$ is found in the acid [5].

$$\begin{matrix}CH_2-COOCH_3\\ |\\ CH_2-COOH\end{matrix} + H_2\overset{18}{O} \overset{H^+}{\rightleftarrows} \begin{matrix}CH_2-C\overset{18}{O}OH\\ |\\ CH_2-COOH\end{matrix} + CH_3OH$$

Thus, in the esterification reaction the bond (a) between the hydroxyl and the carbon is broken in the acid molecule

$$RCO \overset{(a)}{-} O \overset{(b)}{-} H$$

---

* Dedusenko and Brodsky showed [3] that the reaction of acid anhydrides with alcohols proceeds according to the equation:

$$R-\underset{\underset{O}{\|}}{C}-\boxed{O-\underset{\underset{O}{\|}}{C}-R+H}-\overset{18}{O}-R' \longrightarrow R-\underset{\underset{O}{\|}}{C}-\overset{18}{O}-R' + H-O-\underset{\underset{O}{\|}}{C}-R$$

and not according to

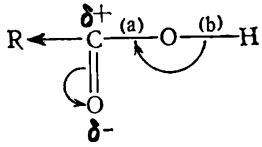
$$RCOO\ \boxed{COR+HO}-R' \longrightarrow RCOOR'+HOCOR$$

while the bond (b) between hydrogen and oxygen

$$R' \overset{(a)}{\text{—}} O \overset{(b)}{\text{—}} H$$

is broken in the alcohol molecule. The relative strength of bonds (a) and (b) depends on the electronegativity of groups R and R'.

If the R group in the acid is strongly electronegative, preferred scission of (b) may be expected on esterification because this bond is weakened by the withdrawal of electrons by the oxygen and the R group:



Similarly, if the group R' in the alcohol molecule is strongly electropositive, preferred scission of bond (a) may be expected.

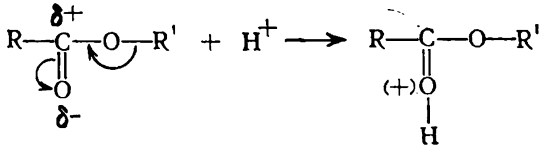
Thus, in general, the reaction of esterification-hydrolysis may follow either mechanism I or II, depending on the electronegative properties of the groups R and R'.

## 6-2 ACID HYDROLYSIS OF ESTERS

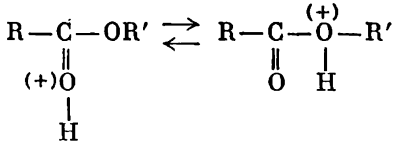
Esters are weakly basic substances. Many of them give a double depression of the freezing point in 100% sulphuric acid solution. This is probably due to the fact that two particles form when the ester reacts with sulphuric acid:

$$R{-}COOR' + H_2SO_4 \rightleftarrows [R{-}COOR']H^+ + HSO_4^-$$

The proton evidently adds to the oxygen atom of the carbonyl group

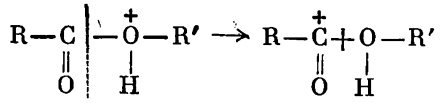


It is natural to postulate the existence of tautomerism between the two cations:

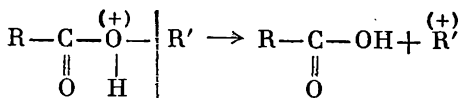


(A) (B)

Cation (B) may decompose further with severance of the acyl-oxygen bond

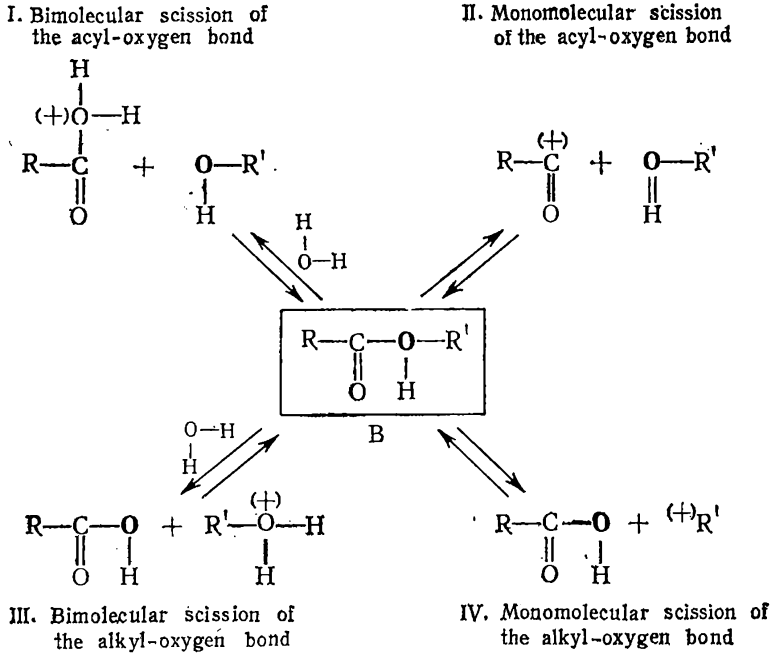


or with rupture of the alkyl-oxygen bond



Both types of decomposition may proceed either as monomolecular or bimolecular processes with the participation of one molecule of water.

All the possible transformations of cation (B) in the hydrolysis reaction may be represented by the following diagram*:


I. Bimolecular scission of the acyl-oxygen bond
II. Monomolecular scission of the acyl-oxygen bond
B
III. Bimolecular scission of the alkyl-oxygen bond
IV. Monomolecular scission of the alkyl-oxygen bond

Of the four given mechanisms of transformation of cation (B), mechanism III has hardly been studied.

**Bimolecular Acid Hydrolysis Involving Scission of the Acyl-Oxygen Bond.** That water reacts with the product of addition of proton to an ester (with cation B) follows from the fact that hydrol-

* Bold type indicates the ether oxygen as distinct from the carbonyl oxygen.

ysis of an ester in acetone with an equimolecular quantity of water is a second-order reaction. Since the rate of hydrolysis of esters depends also on the concentration of the acid used as a catalyst, the overall equation of the reaction rate is

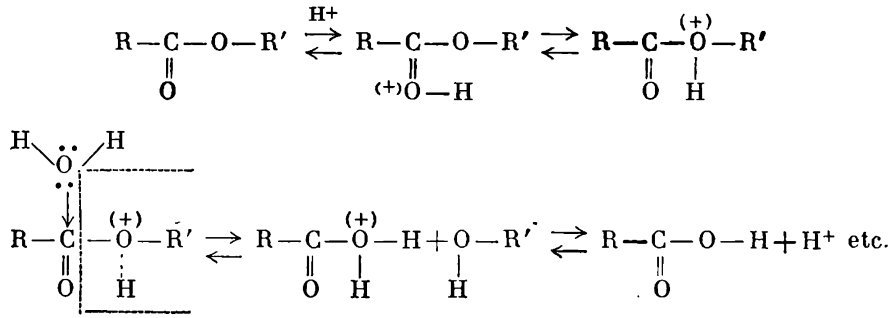
$$v = k\,[\text{ester}]\,[H^+]\,[H_2O]$$

In aqueous solution, where the water concentration is constant, the equation is more simple:

$$v = k_1\,[\text{ester}]\,[H^+]$$

It was shown that a large number of esters are hydrolyzed according to this equation.

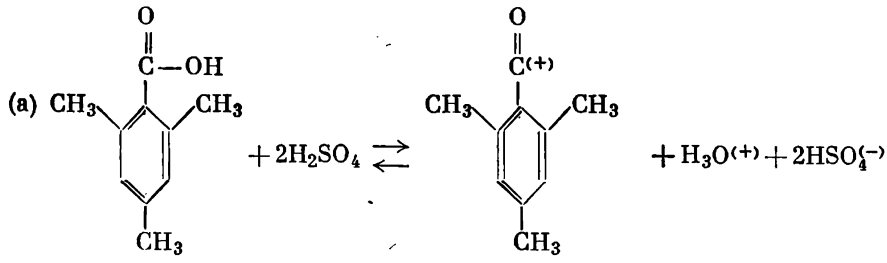
The following mechanism of bimolecular acid hydrolysis (and esterification, respectively) is in agreement with the above data:

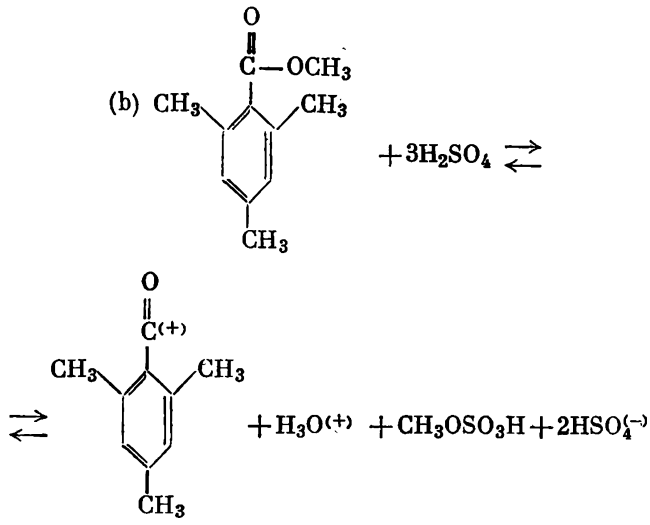


**Monomolecular Acid Hydrolysis Involving Scission of the Acyl-Oxygen Bond.** At least one case is known where the cation (B) decomposes independently of whether it is attacked by a water or an alcohol molecule. This is the formation or hydrolysis of esters of 2,4,6-trimethylbenzoic acid in sulphuric acid solution.

It is known from cryoscopic investigations that free trimethylbenzoic acid exhibits a four-fold, and its methyl ester a five-fold, melting point depression in sulphuric acid solution.

The most likely explanation of such a depression is that acyl carbonium ions are formed:

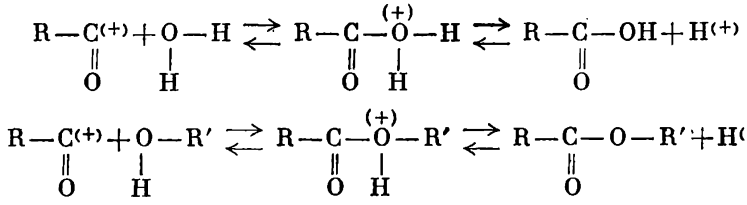




It is logical to assume that the product of addition of a proton to an ester (cation B) also decomposes to form an acyl cation $R-C^{(+)}=O$ in the course of the reaction.

Such an assumption is borne out by experiment. For instance, when a sulphuric acid solution of methyl 2,4,6-trimethylbenzoate is poured into ice water, 2,4,6-trimethylbenzoic acid is formed in a quantitative yield*. If a sulphuric acid solution of 2,4,6-trimethylbenzoic acid is poured into methanol, the yield of the ester formed (methyl 2,4,6-trimethylbenzoate) is 78%.

The smooth and easy course of the last two reactions is readily explained by the interaction of water and alcohol with the reactive acyl cation:



Neither water nor alcohol cause any change in benzoic acid and ethyl benzoate in sulphuric acid solution. This shows that benzoyl cation does not form under the conditions of formation of 2,4,6-trimethylbenzoyl ion.

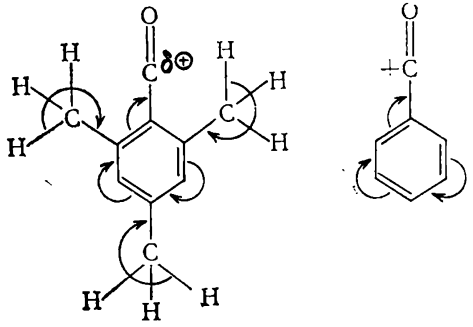
---

* For proof of the fact that the acyl-oxygen bond is ruptured during the hydrolysis of methyl trimethylbenzoate see [6].

The relative ease of formation of the trimethylbenzoyl cation is due to the electron-donor action of methyl groups, resulting in partial neutralization of the positive charge on the carbonyl carbon atom. In the benzoyl cation the charge is localized largely on the carbonyl carbon.

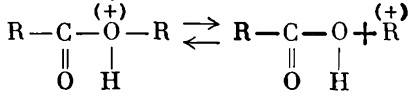
That is why the trimethylbenzoyl cation is more stable and forms more readily than the benzoyl cation.

It is very important that the solution be highly acidic. In water alcohol solution containing traces of acid the hydrolysis of methyl



trimethylbenzoate is bimolecular. However, this bimolecular reaction proceeds so slowly (mainly because of steric hindrance) that only traces of 2,4,6-trimethylbenzoic acid are formed.

**Monomolecular Acid Hydrolysis Involving Rupture of an Alkyl-Oxygen Bond.** In the monomolecular decomposition of the intermediate cation B involving rupture of an alkyl-oxygen bond

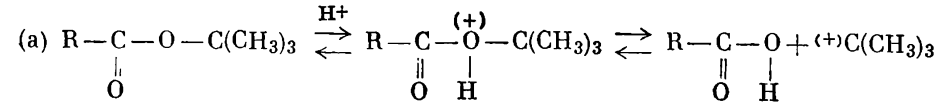


a carbonium ion is formed which must undergo the characteristic secondary transformations (rearrangement, alkene formation, etc.).

Experimental data are in agreement with this assumption.

Thus, hydrolysis of a number of allyl esters is accompanied by rearrangement, which indicates that the alkyl-oxygen bond is ruptured in this reaction.

Acid hydrolysis of *tert*-butyl esters of fatty acids results in isobutylene, and alcoholysis—in ether as a by-product. These are natural products of transformation of the carbonium ion $(CH_3)_3\overset{+}{C}$



(b) $(CH_3)_3C^{(+)} \rightleftarrows \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C=CH_2 + H^+$

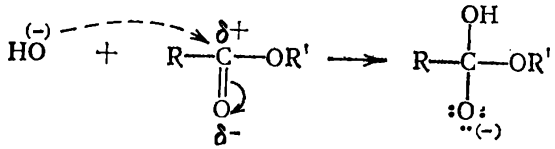
(c) $(CH_3)_3C^{(+)} + H-OR' \rightleftarrows (CH_3)_3C-O-R'^{*} + H^+$

It should be noted that like the monomolecular hydrolysis of alkyl halides ($S_N1$), the monomolecular hydrolysis of esters proceeds more readily in the presence of alkyl radicals, possessing high electron-donor properties, such as the tertiary butyl radical (cf. page 110).

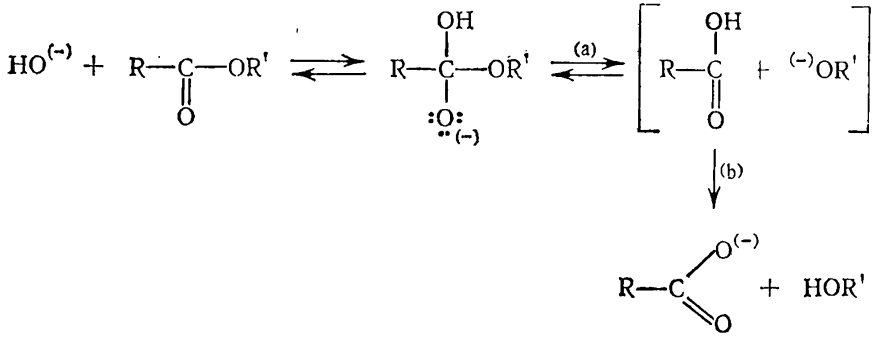
## 6-3 ALKALINE HYDROLYSIS OF ESTERS

Alkaline hydrolysis of esters is a bimolecular reaction.

The first stage of the alkaline hydrolysis of esters consists in the hydroxyl ion attacking the carbonyl carbon which carries a partial positive charge.



The intermediate anion formed may decompose either into the original reactants or with elimination of its alkoxyl anion.



Alkaline hydrolysis is irreversible because of the irreversibility of the stage (b).

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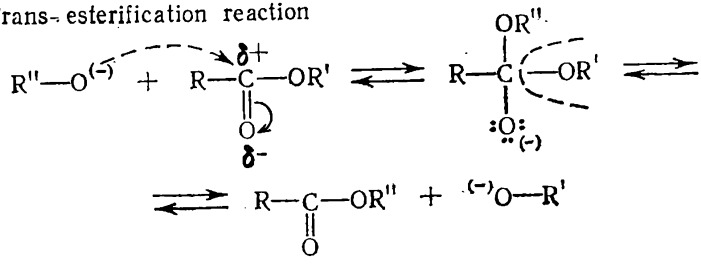
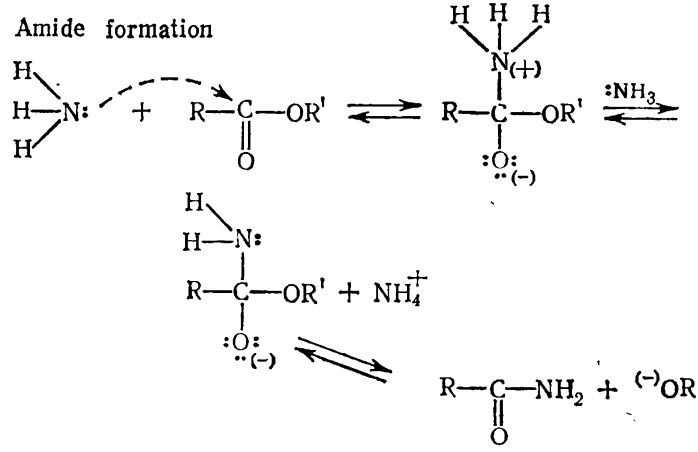
* Special experiments have shown it impossible to form ethers by the reaction of trimethylcarbinol with another alcohol (R'OH) under the conditions of the reaction.

The mechanism of trans-esterification (or ester interchange) reactions and of the formation of amides from esters under the action of ammonia is similar to the above:

Trans-esterification reaction

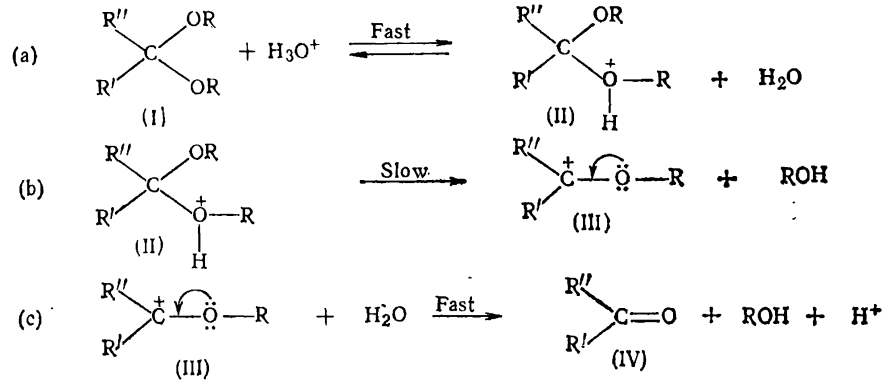


Amide formation



## 6-4 HYDROLYSIS OF ACETALS

Acetals are quite stable in alkaline media, but are readily hydrolyzed in the presence of acids. The mechanism of hydrolysis may be illustrated by the following scheme [7]:



According to this scheme the ethereal oxygen atom is attacked by the hydronium ion ($H_3O^+$); the acetal molecule (I) is transformed into the oxonium compound (II). The latter slowly decomposes (the rate-limiting step of the entire process) into the cation (III) and a molecule of alcohol. Finally, the intermediate cation (III) decomposes rapidly forming the end carbonyl compound (IV).

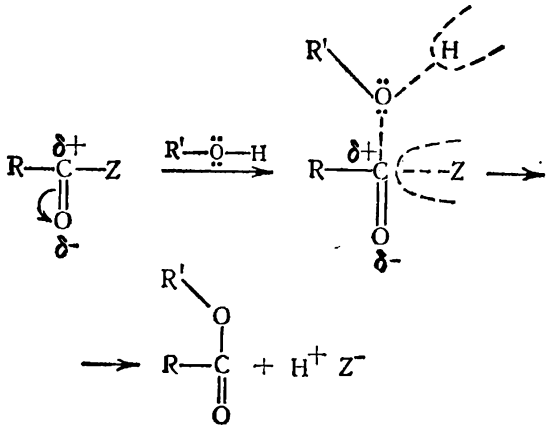
The effect of the nature of the R′ and R″ groups is in agreement with the above-given mechanism. A systematic study of the effect of polar and steric factors on the rate of hydrolysis of acetals was carried out by Kreevoy and Taft [8].

## 6-5. ACIDS AND THEIR DERIVATIVES AS ACYLATING AGENTS

It is known that the acylating power of carboxylic acid derivatives follows the following sequence:

*Acyl halides* > *acid anhydrides* < *acids* > *esters*

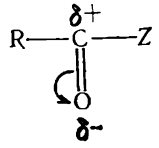
This phenomenon may be accounted for as follows. If acid derivatives are designated RCOZ (Z being halogen, OOCR′, OH, OR′) the general acylation mechanism of, say, alcohols may be represented as follows:



Evidently, the acylation reaction consists in an alcohol (or some other acylated substance) attacking the positively charged carbon of the carbonyl group and forming a bond with the free electron pair of the alcohol oxygen. Simultaneously in the transition state, Z and H are eliminated as an anion and a cation, respectively.

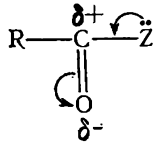
It is clear that if one and the same substance is acylated by different acylating agents the reaction will proceed the faster, the greater

the partial positive charge ($\delta+$) on the carbonyl carbon:



If the same radical (R) is used, the magnitude of the positive charge will depend on the electronegativity of Z.

The more electronegative Z is, the harder it will be to shift its electrons toward the acyl radical,



and, therefore, the larger the charge on the carbonyl carbon.

Conversely, the easier the electrons can be shifted from Z toward the acyl group, the smaller the positive charge on the carbonyl carbon atom*.

An idea of the sequence of electronegativity of the anions Cl, R'COO, OH and OR' can be had from a comparison of their hydrogen compounds:

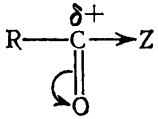
H : Cl
H : OOCR'
H : OH
H : OR'

In the hydrochloric acid (strong acid) molecule the electrons are drawn the farthest away from the hydrogen, less in the carboxylic acid molecule (weak acid), still less in water, and least in the alcohol molecule (water is more acid in nature than alcohol).

Therefore, the electronegative properties of the above groups fall into the following sequence:

$$Cl > OOCR' > OH > OR'$$

* Exactly the same effect would be observed in those (quite feasible) cases when the Z groups (all or only some) are more electronegative than the acyl group RCO. In these cases the more electronegative Z will attract the electrons from the carbonyl carbon more strongly



increasing its positive charge. With less electronegative Z this action will be weaker, resulting in a smaller positive charge on the carbonyl carbon.

Thus, we come to the conclusion that the magnitude of the positive charge on the carbonyl carbon atom and, therefore, its acylating power, must decrease in the following sequence:

$$R-\overset{\overset{O}{\|}}{C}-Cl > R-\overset{\overset{O}{\|}}{C}-OCOR' > R-\overset{\overset{O}{\|}}{C}-OH > R-\overset{\overset{O}{\|}}{C}-OR'$$

This is in agreement with experimental data.

Acyl halides are the strongest acylating agents, anhydrides are somewhat weaker*; organic acids (in the absence of mineral acids) acylate alcohols very slowly.

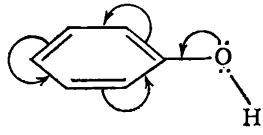
Esters are the weakest acylating agents; in the absense of mineral acids they acylate water (hydrolysis reaction) very slowly.

In the presence of hydrogen ions acids and esters become much stronger acylating agents, but the catalytic reactions which take place in this case are of a different nature and follow a fundamentally different mechanism (pages 418-422).

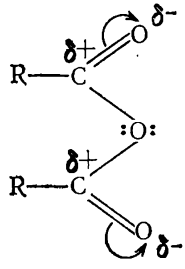
The rate of the acylation reaction must, naturally, depend also on the structure of acylated substances.

It is known, for example, that phenols do not form esters when acted on by fatty acids at moderate temperatures but are easily acylated by acyl halides.

This is due to the fact that in the phenol molecule the free electrons of the oxygen atom are displaced towards the benzene ring



* It should be noted that the reason why anhydrides have a lower acylating power than acyl halides can be understood if it is taken into consideration that the oxygen (which is less electronegative than halogen) is linked to two acyl groups:



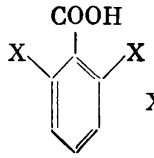
Naturally, the positive charges of the two carbonyl carbons can be neutralized only insignificantly by the free electrons of a single oxygen atom.

which impedes attack on the carbonyl oxygen of the carboxylic acid and the formation of a new bond with the free electron pair of the oxygen atom of phenol*.

But in acyl chloride the positive charge on the carbonyl carbon is larger, and it reacts with phenol.

## 6-6 STERIC HINDRANCE IN THE ESTERIFICATION-HYDROLYSIS REACTION

As shown by Victor Meyer [9], *ortho*-disubstituted benzoic acids are esterified by alcohol and HCl very slowly or not at all



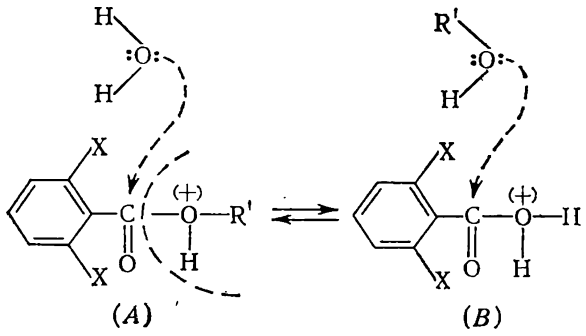

$X = NO_2$, Cl, Br, I, $CH_3$, OH, F

Esters of these acids can easily be obtained from the reaction between their silver salts and alkyl halides, but these esters are quite stable toward saponifying agents: they hydrolyze very slowly. *Ortho*-disubstituted phenylacetic acids, in which the carboxyl group is not directly linked to the benzene ring, on the contrary, esterify readily and their esters are hydrolyzed with ease.

This effect of substituents on the reactivity of *ortho*-disubstituted benzoic acids and their esters cannot be ascribed to the electronic effects of the substituents, because electron-donor and electron-acceptor groups have the same effect. The cause lies in steric hindrance.

Esterification of benzoic acids with alcohol in the presence of HCl (and acid hydrolysis of the corresponding esters) is a bimolecular reaction involving rupture of the acyl-oxygen bond:

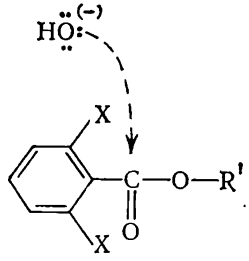
* Until Aelony's publication on direct esterification of phenols by fatty acids [8a], it was considered that phenols could not be esterified by fatty acids.



(A) (B)

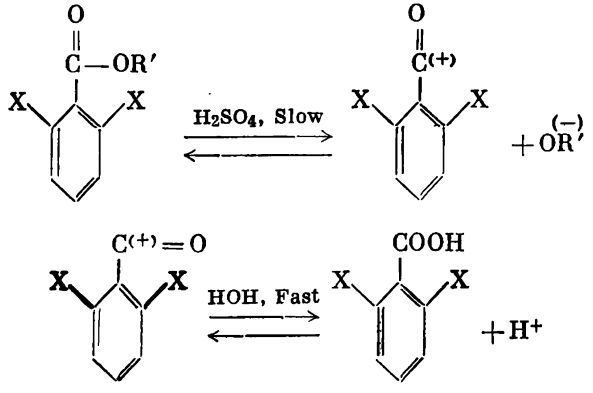
The substituents X cause steric hindrance in the attack of water and alcohol molecules on the carbonyl carbon of the ester (A) and the acid (B) respectively.

There is a similar hindrance in alkaline hydrolysis



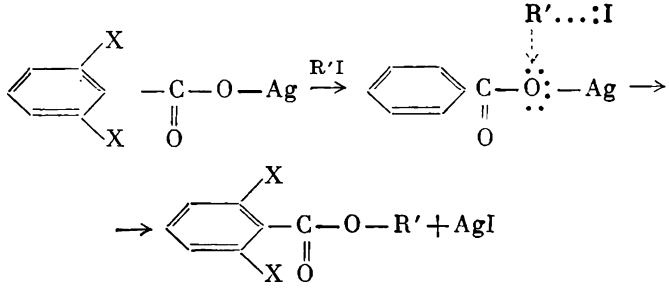
where the carbonyl carbon of the ester group is attacked by a hydroxyl ion.

When esters of *ortho*-disubstituted benzoic acids contain electron-donor substituents, they may be hydrolyzed by dissolving them in concentrated sulphuric acid and pouring the resulting solution into water. This causes the monomolecular reaction.



The *ortho*-disubstituted benzoyl cation is naturally attacked more easily by water than the undissociated ester group in bimolecular hydrolysis reactions. The role of electron-donor groups consists in partially neutralizing the positive charge of the carbonyl cation and lowering its energy, so that it forms comparatively easily (page 422).

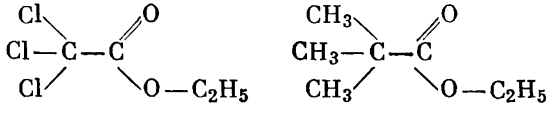
Finally, it should be noted that the ready formation of esters from silver salts of *ortho*-disubstituted benzoic acids and alkyl halides is easy to understand because the cation of the alkyl halide attacks the oxygen of the carboxyl groups and not the sterically hindered carbon atom:



## 6-7 SOME QUANTITATIVE RELATIONSHIPS OF THE DEPENDENCE OF REACTIVITY ON STRUCTURE. SEPARATION OF ELECTRONIC AND STERIC FACTORS*

In general, the reactivity of substances depends on the peculiarities of their electronic structure and on steric factors. A quantitative evaluation of the roles of electronic and steric factors is a complex problem, though many examples can be given where reactivity is due either exclusively to electronic or exclusively to steric factors.

For instance, the alkaline hydrolysis of ethyl trichloroacetate (I) proceeds about 8 million times faster than the alkaline hydrolysis of ethyl trimethylacetate (II).

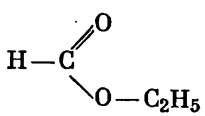


(I) (II)

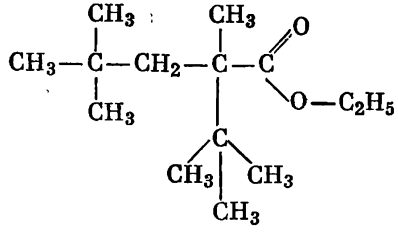
This tremendous difference in reaction rates is due almost entirely to electronic factors: to the greater electron-acceptor power of the trichloromethyl group in comparison with the *tert*-butyl group.

* See [10, 11] for reviews.

The difference in the rates of acid hydrolysis of ethyl formate III) and methyl neopentyl-*tert*-butyl acetic acid (IV) is an example of difference in reactivity due almost entirely to steric factors.



(III)



(IV)

Ester IV is hydrolyzed 100,000 times slower than ester III.

### 6-7.1 Hammett Equation

Reactivities of substances can be characterized quantitatively either by the free energy $\Delta F_i$ (if equilibrium is considered) or by the free energy of activation $\Delta F_{\neq i}$ (if the reaction rate is considered). It is known that $\Delta F = -2.303\ RT \log K$, and $\Delta F_{\neq} = -2.303\ RT \log K - 2.303 \log \frac{kT}{n}$ (where $K$ is the equilibrium constant and $k$ is the rate constant). Therefore, the logarithm of the equilibrium constant $\log K$ or the logarithm of the rate constant $\log k$ are convenient chemical measures of the free energy within a series of uniform reactions.

If the $\log k_i$ values of different series of reactions are related by a linear dependence of the type

$$(\log k_i)_m = \alpha + \beta\,(\log k_i)_n \qquad \text{(I)}$$

where $m$ and $n$ signify different series of reactions and $\alpha$ and $\beta$ are constants), the changes of free energies are in linear dependence.

If one of the reactions of a given series is chosen as a standard and the equilibrium constant or rate constant of this reaction is designated by $K_0$, the following expression can be obtained for the linear dependence of the free-energy change:

$$(\log K_i/K_0)_m = \text{const}\,(\log K_i/K_0)_n \qquad \text{(II)}$$

The value $\log K_i/K_0$ is then a measure of the change in free energy in passing from the standard reaction to the $i$-reaction within the given series of uniform reactions.

Hammett used the rule of linear dependence between changes of free energies to correlate the reactivities of *meta*- and *para*-substituted benzene, because the effect of these derivatives (as distinct

from *ortho*) on the reaction rates or on the equilibria depends solely on the polar effect of the substituents (and not at all on steric factors).

Designating const $= \rho$ in expression (II) and assuming that $\rho = 1$ for the reaction series selected as a standard (dissociation of substituted benzoic acids in water at 25°), Hammett derived the correlation:

$$\log (K_i/K_0) = \sigma_i \rho \qquad \text{(III)}$$

where $\sigma_i = \log K_i/K_0$, and $K_i$ and $K_0$ are the ionization constants of the substituted and unsubstituted benzoic acids, respectively.

Rewritten in a more general form (IV), this correlation

$$\log (K/K_0) = \sigma\rho \qquad \text{(IV)}$$

is known as the *Hammett equation* [12, 13], where $\sigma$ is the substituent constant, independent of the reaction. It is a measure of the polar effect of the *meta*- or *para*-substituents in question with respect to the hydrogen atom in any reaction.

TABLE 6-3

**Typical Values* of $\sigma$**

| Substituent | $\sigma$ | | Substituent | $\sigma$ | |
|---|---|---|---|---|---|
| | *Para* | *Meta* | | *Para* | *Meta* |
| $NH_2$ | −0.660 | −0.161 | Br | +0.232 | +0.391 |
| $N(CH_3)_2$ | −0.83 | −0.211 | I | +0.276 | +0.352 |
| OH | −0.357 | −0.002 | $COCH_3$ | +0.516 | +0.306 |
| $OCH_3$ | −0.268 | +0.115 | $CO_2C_2H_5$ | +0.522 | +0.398 |
| $OC_6H_5$ | −0.028 | — | $CF_3$ | +0.551 | +0.415 |
| $CH_3$ | −0.170 | −0.069 | CN | +0.628 | +0.678 |
| $t$-$C_4H_9$ | −0.197 | −0.120 | $SO_2CH_3$ | +0.728 | +0.647 |
| H | −0.000 | −0.000 | $NO_2$ | +0.778 | +0.710 |
| F | +0.062 | +0.337 | $\overset{+}{N}(CH_3)_3$ | +0.859 | +0.904 |
| Cl | +0.227 | +0.373 | | | |

* For a more complete list of $\sigma$ values see [10, 13].

Some typical $\sigma$ values are given in Table 6-3.

The proportionality constant $\rho$ depends on the nature and conditions of the reaction; it is a measure of the sensitivity of a given series of reactions to the introduction of polar substituents.

In 1953, the Hammett equation and available ρ and σ values overed about 42,000 rate and equilibrium constants. For 3,180 eactions the Hammett equation calculations had an average deviaion of ±15% from the experimentally determined rate or equiibrium constants [13]. Thus, though the Hammett equation is not xact, it is applicable as a reliable first approximation.

Equation (IV) shows that the corresponding polar effect of the ubstituent on the difference of free energies changes proportionally n passing from one series of reactions to another, i.e., there is a corelation independent of the reaction mechanism, the attacking eagent, solvent, temperature and the nature of the functional roups participating in the initial, transition or final states. Although hese variables determine the value of the constant ρ, the correation of data to Equation (IV) does not depend on it.

The substituent constant σ is not always independent of the ature of the reaction. Hammett discovered that the value for he *p*-$NO_2$ group, obtained from data on the ionization of *p*-nitroenzoic acid does not fit into Equation (IV) in the case of aniline r phenol derivatives. However, if use is made of the σ value of that roup, based on the relative constant of ionization of *p*-nitroaniline n water at 25°, for all reactions of aniline and phenol derivatives or which experimental data are available, satisfactory agreement with the Hammett equation is observed. Duality of σ values has been assumed in certain other substituents as well.

Let us use the Hammett equation for prediction purposes. Suppose it is required to predict the stability of an 0.1 *M* solution of *p*-nitrobenzenesulphochloride in benzene containing 0.1 *M* aluminium chloride at 30°. The rate of the Friedel-Crafts reaction which occurs in this reaction mass is not known, but it is known for the unsubstituted benzenesulphochloride and for some of its *meta*- and *para*-substituents. We find in the literature [14] that $\log K_0 = -4.31$ and $\rho = -1.80$. Taking the σ value for *para*-$NO_2$ group as +0.778 (Table 6-3), we obtain

$$\log K = (-1.80)(+0.778) - 4.31 = 5.71 \text{ sec}^{-1}$$

Hence, the time required for conversion of half of the *p*-nitrobenzenesulphochloride in benzene solution is about 6,000 min. This is quite a reliable figure.

In using the Hammett equation for prediction purposes it is generally easier to obtain the σ value for the desired substituent than the ρ value for the necessary conditions of reaction.

However, the ρ value may be obtained as follows. A dependence curve is plotted for the experimental values of log *K* or log $(K/K_0)$ vs. σ values for four or more substituted and unsubstituted benzene derivatives. If the series is selected adequately (covering broad values of σ and avoiding duality of σ values) the slope of the straight line obtained gives the ρ value.

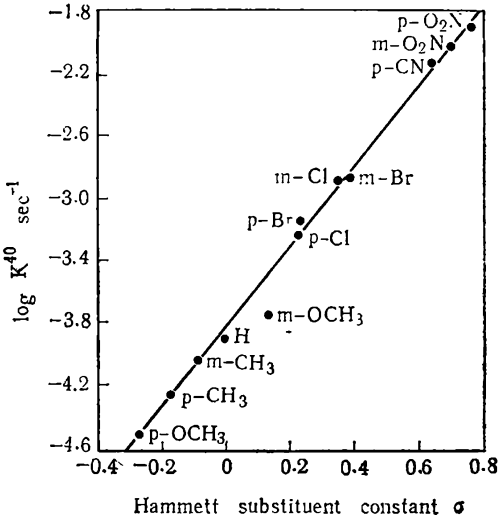



FIGURE 6-1 Determination of the ρ constant for methanolysis of *meta*- and *para*-substituted *l*-menthyl benzoates.
Slope $\rho = +2.552$; intercept log $K_0 = -2.859$

TABLE 6-4

**Values of ρ for Some Reactions**

| No. | Reaction | ρ |
|---|---|---|
| 1 | Ionization of benzoic acids in water at 25° | 1.000* |
| 2 | Ionization of benzoic acids in ethanol at 25° | 1.957* |
| 3 | Ionization of phenols in water at 25° | 2.113* |
| 4 | Addition of HCN to benzaldehyde in water at 20° | 1.492* |
| 5 | Addition of HCN to benzaldehyde in ethanol at 20° | 2.239 |
| 6 | Ionization of triarylchloromethanes in $SO_2$ at 0° | −3.574* |
| 7 | Alkaline hydrolysis of methyl benzoate in 60% aqueous acetone at 0° | 2.460 |
| 8 | Acid hydrolysis of ethyl benzoates in 60% ethanol at 100° | 0.144 |
| 9 | Hydrolysis of benzyl chlorides in 50% aqueous acetone at 60° | −1.688 |
| 10 | Benzoylation of aromatic amines in benzene at 25° | −2.781 |
| 11 | *cis-trans*-Isomerization of substituted azobenzenes in $C_6H_6$ at 25° | −0.610 |
| 12 | Reduction of nitrobenzene with $SnCl_2$ in water at 90° | 1.149 |
| 13 | Bromination of acetophenone in the side chain in water at 25° | 0.417 |
| 14 | Decomposition of substituted benzoyl peroxides in acetophenone at 80° | 0.374 |

* These values of ρ have been calculated from equilibrium constants; the rest are based on rate constants.

The reaction constant ρ for the trans-esterification reaction between -menthyl benzoate and methanol is determined by way of example n Fig. 6-1.

The larger the absolute value of ρ, the more sensitive is the reaction in question to the polar effects of substituents.

The ρ values [13] for some reactions are given in Table 6-4.

The problem of reactivity is much more complicated when the ubstituents are situated close to the reaction centre. Such is the ase, for instance, with *ortho*-substituted benzenes and a great ariety of reactions of aliphatic compounds. In these cases the Iammett equation is inapplicable, because steric factors begin o play an important part alongside polar factors.

### 6-7.2 Polarity Constants of Substituents for Groups Linked Directly with the Reaction Centre. Taft Equation [8, 15-19].

The problem of the quantitative correlation between the structure nd reactivity of aliphatic hydrocarbons becomes simpler when he reactive centre is not part of the conjugated system, and if, esides, the magnitude of steric interaction of the substituents with he reaction centre does not change noticeably during the reaction.

Of course, these limitations narrow down the circle of reactions overed. A large number of reactions in the aliphatic series are known o satisfy these conditions.

In these cases, as in the reactions of *para*- and *meta*-substituted ompounds of the benzene series, changes in the rate and equilibrium onstants (within one group of reactions) are determined only by the lectron-donor and electron-acceptor properties of the substituents.

The rate and equilibrium constants of such reactions are in agreement with an equation, which at first glance is identical with he Hammett equation:

$$\log (K/K_0) = \overset{**}{\sigma}\rho$$

This is the *Taft equation.*

Like in Hammett equation, $K$ is the rate or equilibrium constant f some compound of a given reaction series; $K_0$ is the corresponding onstant for the compound taken as the standard (usually a methyl ompound), ρ* is a constant analogous to constant ρ in the Hammett quation, and σ* is the polar substituent constant, reflecting the lectron-donating or -withdrawing effect of the substituent, realized hrough a chain of single bonds (the inductive effect).

As was indicated above, the values of the constants σ for the Iammett equation were obtained on the basis of ionization constant ieasurements for substituted benzoic acids in water.

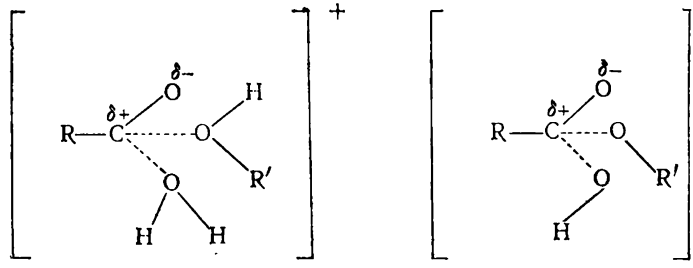
Satisfactory values for σ* cannot be obtained by studying the ionization constants of aliphatic acids, because not all aliphatic acids obey Brönsted's catalytic rule[1]. This is apparently due to the fact that large substituents may act on the carboxylate ion by "intramolecular solvation"; besides there may be no correlation between the degree of such an interaction and the polarity of the substituents.

Reliable σ* values for substituents can be obtained by measuring the rates of acidic and basic hydrolysis of esters containing substituents R linked directly with the carbalkoxyl group R — COOR'.

The choice of these objects for determining σ* constants, which are quantitative characteristics of the inductive effect, is due to the following. If the values of the Hammett constants for the alkaline and acidic hydrolysis of benzoic acid esters are compared (Table 6-4, reactions 7 and 8), it becomes evident that alkaline hydrolysis is very sensitive to the electronic effects of the substituents (ρ has a high value, 2.460), while acidic hydrolysis is practically insensitive to the electronic effects of the substituents (ρ = 0.144); the ρ value is close to zero. For example, the acid hydrolysis rates of *p*-nitrobenzoic and *p*-methoxybenzoic acids differ only by about 12%.

At the same time, the acid hydrolysis rate of fatty acid esters varies considerably depending on the substituents. There is no reason to think that acid hydrolysis of fatty esters should be more sensitive to polar effects than acid hydrolysis of aromatic esters.

Therefore the sensitivity of acid hydrolysis of fatty esters to the nature of the substituents must depend on *steric factors*. For this reaction the logarithm of ratios of the rate constants of the substituted and standard esters $\log (K/K_0)_A$ becomes a measure of the increment $\Delta F$ due to steric effects.



(I) (II)

[1] Brönsted's catalytic rule

$$\log K_{cat} = a \log K_a + b$$

expresses the relation between the acid constants of acids $K_a$ and their catalytic constants $K_{cat}$ for given acid-catalyzed reactions.

As the transition states in bimolecular acid hydrolysis (I) and bimolecular alkaline hydrolysis (II) differ only by two protons, Taft assumed that the steric effects in both types of reactions are essentially the same.

Since both steric and polar effects are important in alkaline hydrolysis, the expression $\log (K/K_0)_B$ is in this case a measure of the increment $\Delta F$ due to the combination of both these effects. This being so, the difference $\log (K/K_0)_B - \log (K/K_0)_A$ is a *measure* of the *polar effect* or, more precisely, of the *inductive effect*, because we are considering reactions of compounds whose reactive centres are not links in chains of conjugated bonds.

Taft expressed $\sigma^*$ as follows:

$$\sigma^* = \frac{1}{2.5}\left[\log \left(\frac{K}{K_0}\right)_B - \log \left(\frac{K}{K_0}\right)_A\right]$$

where the subscripts $A$ and $B$ refer to acid and base hydrolysis, respectively. The value $K_0$ is the specific rate of the corresponding hydrolysis of the acetic acid ester (R= $CH_3$), chosen as the standard. The purely arbitrary factor 2.5 was introduced so that Taft's constant should lie approximately within the same scale as Hammett's $\sigma$ constants.

The $\sigma^*$ values for some substituents[1] and the $\rho^*$ values for some reactions of the aliphatic series are given in Tables 6-5 and 6-6, respectively.

TABLE 6-5

**Taft Polar (Inductive) $\sigma^*$ Constants**

| Substituent | $\sigma^*$ | Substituent | $\sigma^*$ | Substituent | $\sigma^*$ |
|---|---|---|---|---|---|
| $CH_3$ . . . . . | 0.000 | $C_6H_5CH_2$ . . | +0.220 | $C_6H_5—C\equiv C$ | +1.35 |
| $C_2H_5$ . . . . . | −0.100 | H . . . . . | +0.490 | $CH_3CO$ . . . | +1.65 |
| $(CH_3)_2CH$ . . | −0.190 | $C_6H_5$ . . . . | +0.600 | $Cl_2CH$ . . . | +1.94 |
| $(CH_3)_3C$ . . . | −0.300 | $ClCH_2$ . . . | +1.05 | $Cl_3C$ . . . . | +2.65 |

It is apparent from these data that substituents fall into the same order of increasing $\sigma^*$ values as their qualitatively established order of increasing inductive effect.

With regard to $\rho^*$ values, it can be said that positive $\rho^*$ values characterize reactions facilitated by electronegative substituents, and negative values of $\rho^*$ characterize reactions facilitated by substituents with a positive inductive effect.

[1] For a more complete list of $\sigma^*$ values see Appendix, Table 17.

It has been established that the dependence of the σ* value on the structure is related to the *rule of additivity* and the *law of extinction of inductive effect.*

The *rule of additivity* is generally strictly adhered to, and may be expressed as follows:

$$\sigma^*(X_1X_2X_3C)=\sigma^*(X_1CH_2)+\sigma^*(X_2CH_2)+\sigma^*(X_3CH_2)$$

Deviations from this rule are observed when $X_1$, $X_2$ and $X_3$ are strongly electronegative substituents.

TABLE 6-6

**Values of Reaction Constants ρ* (Reactions of Aliphatic Series)**

| No. | Reaction | ρ* |
|---|---|---|
| 1 | $R-COOH+H_2O \rightleftarrows RCOO^-+H_3O^+$ | +1.72[1] |
| 2 | $R-COOH+Ph_2CN_2 \rightarrow R-\underset{\underset{C}{\|}}{C}-OCHPh_2+N_2$ (ethanol) | +1.18 |
| 3 | $R-CH_2OH+H_2SO_4 \rightarrow RCH_2-OSO_3H+H_2O$ | +4.60 |
| 4 | $C_6H_5-\underset{\underset{O}{\|}}{C}-CHR_2+Br_2 \xrightarrow{OH^-} C_6H_5-\underset{\underset{O}{\|}}{C}-CBrR_2$ | +1.59 |
| 5 | $R-\underset{\underset{O}{\diagup\diagdown}}{CH}-CH_2+H_2O \xrightarrow{HClO_4} R-\underset{\underset{OH}{\|}}{CH}-CH_3$ (0°) | −1.83 |
| 6 | $R-CH_2Br+PhS^- \rightarrow R-CH_2-S-Ph+Br^-$ ($CH_3OH$, 20°) | −0.61 |

[1] This ρ* value was derived from equilibrium constants; all the rest are based on rate constants.

According to the *law of extinction of inductive effect*, introduction of the methylene group between a substituent X and the reaction centre generally lowers the inductive effect approximately 2.8 times if X is an electronegative substituent.

$$\sigma^*(XCH_2)=\frac{1}{2.8}\sigma^*(X)\pm 0.005$$

If X is a hydrogen atom or an alkyl group, then

$$\sigma^*(XCH_2)=-0.100+\frac{1}{490}\sigma^*(X)\pm 0.01$$

It should be noted that the effect of corresponding substituents upon the reactivity of compounds in reactions of different types is characterized by the same σ* values.

The same σ* values quantitatively characterize the effect of substituents upon certain physical properties of organic substances (for example, upon the infrared frequencies of absorption spectra, dipole moment, etc.

Thus, σ* values are a quantitative expression of the inductive effect of substituents and are quite universal in nature.

### 6-7.3 Steric Constants of Substituents

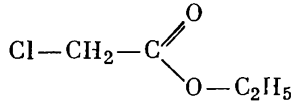
The polar effect of substituents on the rate of hydrolysis of esters was evaluated above. The same data may be used to obtain information on the steric effect of substituents.

Let us first consider initial premises on the basis of which substituents may be expected to exert a steric influence on the rate of hydrolysis of esters.

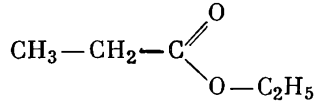
The formation of a transition state whether in the acid or the alkaline hydrolysis of esters (I and II, page 436) involves a transition of the carbonyl carbon atom from the second valence state with valence angles of 120°) to the first valence state (with valence angles of 109°). Therefore in both cases activation should be accompanied by "squeezing" of the substituents. The latter may lead, firstly, to an increase in steric strain (potential energy) in the transition state as a result of repulsion between atoms which are not chemically bound [20] and, secondly, to an increase in the interference of neighbouring groups of atoms with the internal motions of some atoms with respect to others (kinetic energy) [21].

Both of these factors increase the free energy of activation.

Now let us compare the acid hydrolysis of the ethyl esters of chloroacetic (I) and propionic (II) acids.



I

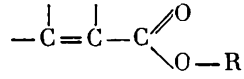


II

The value of $\log (K/K_0)_A$ for I in water at 25° is −0.16; the corresponding value for II is −0.08. The chloromethyl and ethyl groups have nearly the same volumes, but their σ* values are quite different (+1.05 and −0.100, respectively). The fact that the $\log K/K_0)_A$ values for I and II are nearly alike in spite of considerable differences in the values of the polar constants σ* for $ClCH_2$ and $CH_3CH_2$ indicates that the sensitivity of acid hydrolysis to polar

effects is practically zero. Consequently, the relative rates of the reactions in question are practically independent of the polar effect and are determined by nonpolar effects.

In general, nonpolar effects may be due to steric factors and to homolytic conjugation. There are, however, many cases where homolytic conjugation definitely does not take place, for example, in the esters of α, β-unsaturated acids



Taft made use of kinetic data on acid hydrolysis of esters of α,β-unsaturated acids to develop a quantitative measure of the steric constants of substituents [11, 15].

In these cases log $(K/K_0)$ is evidently an almost quantitative measure of purely steric effects related to potential and kinetic energy factors.

This proposition may be expressed by the following equations:

$$\log (K/K_0)_A \equiv E_s; \qquad \log (K/K_0)_B \equiv E_s + 2.48\sigma^*$$

where $E_s$ is an almost quantitative measure of the general steric effect related to the substituent in question with regard to the standard.

Table 6-7 lists some of the values obtained by this method (with methyl group as the reference standard).

It is evident from Table 6-7 that the dependence of the $E_s$ of substituents on their structure has nothing in common with the dependence of the σ* of those substituents on their structure. At the same time it can easily be seen that the nature of the dependence of $E_s$ on the structure of the substituent confirms the steric nature of $E_s$ values.

The additivity rule, which applied in the case of the inductive constants σ*, is not applicable to the steric constants $E_s$. Introduction of a second and a third substituent into the α- or β-positions affects the $E_s$ value more than introduction of the first substituent.

Taft has shown that $E_s$ values are not specific steric characteristics of substituents only in the acid hydrolysis of esters.

In the case of certain other reaction series, for which $\rho^* \approx 0$, the following expression holds:

$$\log (K/K_0) = \delta E_s$$

where δ is the sensitivity constant of the reaction series in question to the steric effect of the substituent.

In some cases where the inductive effect cannot be ignored the following relation exists:

$$\log (K/K_0) = \rho^*\sigma^* + \delta E_s$$

TABLE 6-7

**Steric Constants $E_s$ of Substituents R, Obtained from Kinetic Data on Hydrolysis of Fatty Acid Esters, R — COOR′**

| Substituent R | $E_s$ | Substituent R | $E_s$ |
|---|---|---|---|
| $H(C_6H_5)$— | +1.24 | $(CH_3)(C_6H_5)CH$— | −1.19 |
| $CH_3$ | 0.00 | $(CH_3)_3C$— | −1.54 |
| $C_2H_5$— | −0.07 | I—$CH_2$— | −0.37 |
| $CH_2$—$CH_2$ / $CH_2$—$CH_2$— | −0.06 | $n$-$C_3H_7$— | −0.36 |
| | | $n$-$C_4H_9$— | −0.39 |
| | | $n$-$C_5H_{11}$— | −0.40 |
| $CH_3$—O—$CH_2$— | −0.19 | $n$-$C_8H_{17}$— | −0.33 |
| $ClCH_2$—, $FCH_2$— | −0.24 | $(CH_3)_3C$—$CH_2$—$CH_2$— | −0.34 |
| $BrCH_2$— | −0.27 | $C_6H_5$—O—$CH_2$— | −0.33 |
| $(CH_3)_2CH$— | −0.47 | $C_6H_5$—$CH_2$— | −0.38 |
| $CH_2$—$CH_2$ \ CH— / $CH_2$—$CH_2$ | −0.51 | $(C_6H_5)_2CH$— | −1.76 |
| | | $Br_2CH$— | −1.86 |
| $F_2CH$— | −0.67 | $(n$-$C_3H_7)_2CH$— | −2.11 |
| | | $Br_3C$— | −2.43 |
| $CH_2$ / $CH_2$—$CH_2$ \ CH— / $CH_2$—$CH_2$ \ $CH_2$ | −0.79 | $(CH_3)_2$(neopentyl)C— | −2.57 |
| | | (neopentyl)$_2$CH— | −3.18 |
| $ClCH_2$—$CH_2$— | −0.90 | $(C_2H_5)_3C$— | −3.8 |
| $CH_3$—$CH_2$—$CH(CH_3)$— | −0.98 | $(CH_3)_2$($tert$-$C_4H_9$)C— | −3.9 |
| $CH_3(C_2H_5)CH$— | −1.13 | $CH_3$—$C(CH_3)_2CH_2$— | −4.0 |
| $F_3CH$— | −1.16 | | |

It should be noted that at present there is still insufficient evidence concerning the steric effects of substituents on the reactivity of organic substances.

However, it can already now be asserted that the rule of linear relationship between free energy changes is applicable to the steric component of the quantity determining the total change in free energy of a reaction or of activation[1] in definite reaction series.

At the same time it is evidently clear that there is no universal $E_s$ scale analogous to the σ* scale. Possibly, a set of $E_s$ values for the same substituent should be used for quantitative computation of steric factors in different reaction series.

[1] The total change in the free energy of a reaction or of activation may be resolved into the following series of separate terms, corresponding to the definite structural factors which influence reactivity:

$$\log (K/K_0) = P + H + G + \psi + S$$

where $P$ = inductive effect, $H$ = σ, π-conjugation, $G$ = polar π, π-conjugation, ψ=nonpolar conjugation, and $S$ = steric effects.

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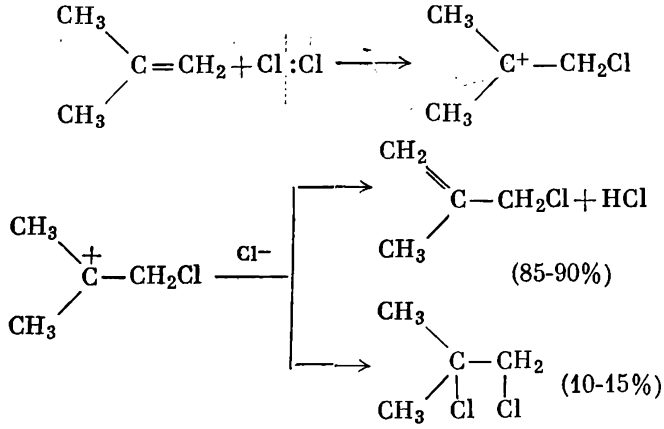
# 7

## SUBSTITUTION REACTIONS AT THE UNSATURATED CARBON ATOM

The most characteristic reactions of unsaturated compounds are those of addition (see Chapter 4). However, substitution at the unsaturated carbon atom often takes place simultaneously with addition and not infrequently plays the predominant part.

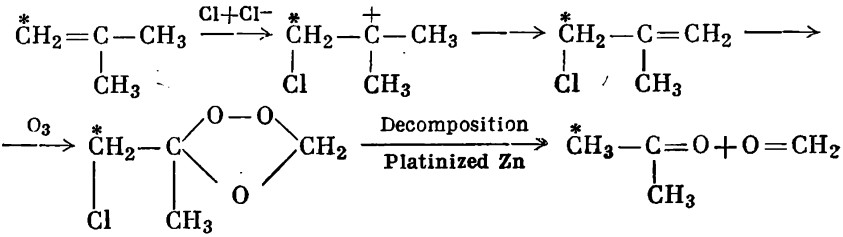
Such reactions, which take place under definite conditions include halogenation, sulphonation, nitration, acylation, diazo coupling, alkylation of olefinic and dienic hydrocarbons.

In most cases substitutions at the unsaturated carbon atom are two-step reactions; they pass through the steps of preliminary addition of the reagent and subsequent elimination of hydrogen halide or water. Thus, chlorination of olefins, say isobutylene, apparently follows the following mechanism [1]:

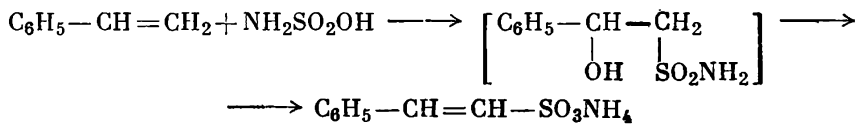



This mechanism is confirmed by a study of the reaction of chlorine at 0° with an excess of isobutene containing $C^{14}$ in its methylene group [2]. The resulting 3-chloro-2-methylpropene-1 was ozonized and the ozonide was decomposed into formaldehyde and acetone. Only the acetone contained $C^{14}$. It is evident that the substitution of chlorine for hydrogen proceeds through an addition step with

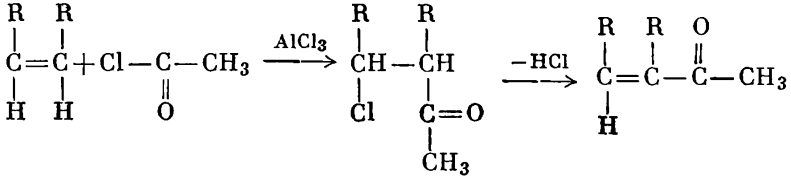
a subsequent change in the position of double bond:



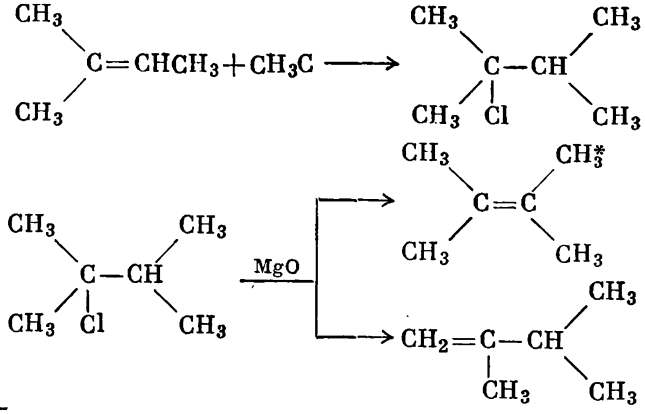
According to Terent'ev [3] sulphonation of olefins and dienes with sulphur trioxide, sulphamic acid, dioxanesulphotrioxide and pyridinesulphotrioxide also proceeds through the steps of addition and elimination, e.g.:



Acylation of olefins in the presence of aluminium chloride follows the mechanism [4]:



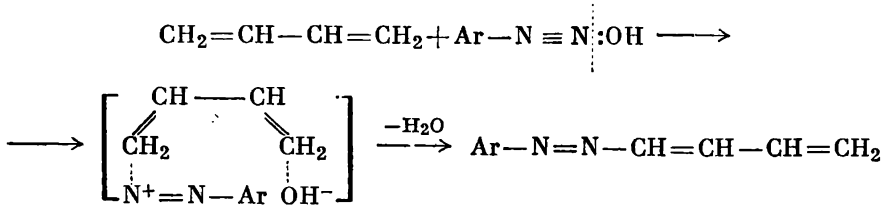
According to El'tekov [5], the methylation of olefins, for instance, trimethylethylene (in the presence of lead, magnesium or zinc oxides), occurs after the mechanism:



* Tetramethylethylene may be methylated further with an excess of methyl chloride.

The reactions of diazonium compounds studied by K. Meyer [6] for diolefins and by Terent'ev [7] for monoolefins pass through a preliminary addition step.

Thus the reaction of aryl diazonium hydroxide with butadiene may be represented by the following scheme:



In the nitration of olefins the elements of nitric acid or nitrogen oxides also add mostly to the multiple bond.

It is obvious that in all the above cases the first step of the reaction is electrophilic addition.

All the above examples may be considered substitution reactions only formally, because actually they are examples of addition-elimination.

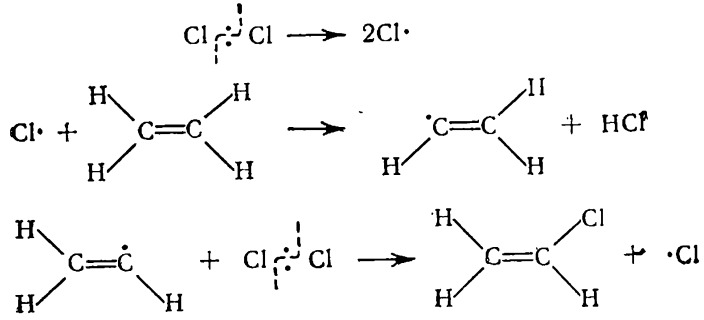
Although it is not easy to distinguish such reactions from reactions of direct substitution, it could be maintained that reactions of direct substitution undoubtedly occur in olefins and their derivatives.

Most of these reactions are of a radical (homolytic) nature.

For instance, the high-temperature (200-600°) vapour-phase halogenation of olefins which has been used industrially since 1937 is undoubtedly a reaction of direct substitution. The presence of small amounts of oxygen favours direct substitution.

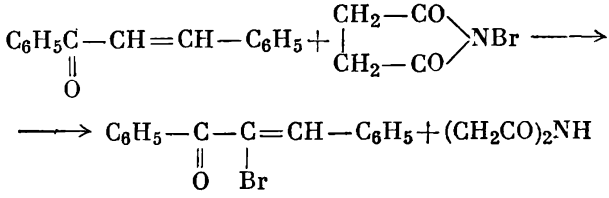
Thus, when ethylene is chlorinated (at 250-350°) in the presence of 0·5% oxygen the yield of vinyl chloride rises from 16% to 93%, while the yield of the addition product drops almost to zero.

The reaction proceeds according to the radical-chain mechanism:



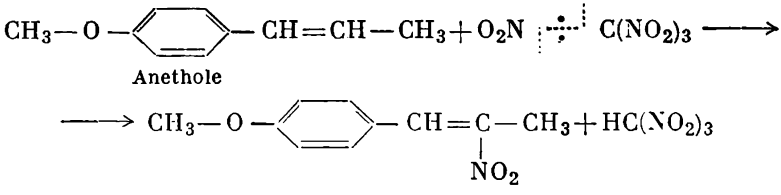
The role of the oxygen is to inhibit the side reaction of addition of atomic halogen to ethylene, because oxygen is a strong inhibitor of the homolytic addition of halogen to olefins (page 270).

Halogenation with *N*-bromosuccinimide is apparently a reaction of direct substitution. For instance, bromination of β-benzoylstyrene with *N*-bromosuccinimide results in β-bromo-β-benzoylstyrene:



This reaction is also of a homolytic nature.

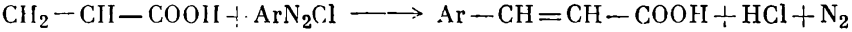
Nitration of olefins under Konovalov's conditions may evidently take place as a reaction of direct substitution, although the yields of the substitution products are low. Nitration with tetranitromethane results in a good yield of substitution products, for instance:



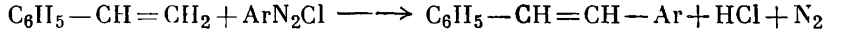

This reaction is also apparently a direct substitution.

Still another direct substitution is, possibly, the reaction of aromatic diazonium compounds with α,β-unsaturated carbonyl compounds in the presence of copper chloride, discovered by Meerwein [8].

For example, under these conditions acrylic acid gives cinnamic acid derivatives:



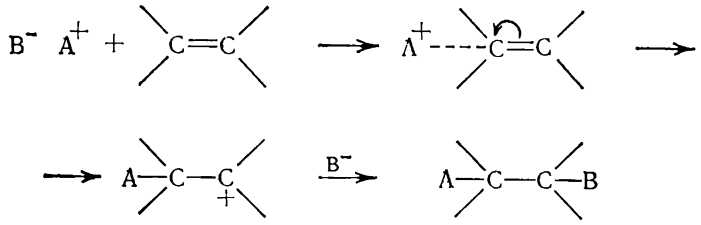
Styrene reacts similarly:



From the above discussion it follows that all known reactions of direct substitution at the unsaturated carbon atom are homolytic radical processes. On the other hand, electrophilic reagents are

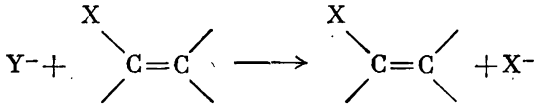
more inclined to add to the multiple bond than to replace atoms linked to the unsaturated carbon atom.

This is clear because π electrons are more mobile than σ electrons. On approaching a molecule, an electrophilic reagent first polarizes it by displacing its π electrons. Then the electrophilic reagent adds at the location of the π-electron pair of the unsaturated compound, this being followed by addition of the nucleophilic reagent:



Naturally, addition of the electrophilic molecule AB may proceed in general without dissociating preliminarily into electrophilic $A^+$ and nucleophilic $B^-$.

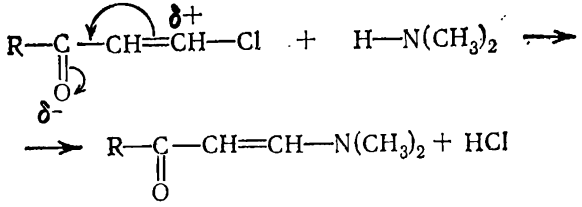
As is known, reactions of nucleophilic displacement



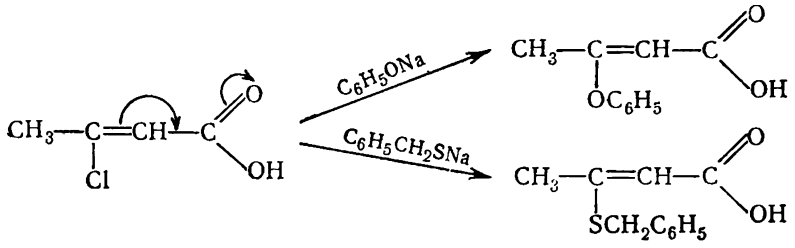
take place with great difficulty and only under stringent conditions in the case of derivatives of the simplest unsaturated hydrocarbons (such as vinyl chloride, propenyl chloride and the like).

Reactions of this type proceed easier in the presence of metallic copper as catalyst, but the reaction mechanism is a radical one in this case.

Atoms (for instance, halogen atoms), bound to an unsaturated carbon, are more mobile when there is an electron-accepting group, such as carbonyl or carboxyl, linked to the neighbouring unsaturated carbon. For example, the chlorine in alkylchlorovinyl ketones is readily replaced by nucleophilic reagents, e. g. [9]:



The chlorine in β-chlorocrotonic and β-chloroisocrotonic acids is mobile for the same reason:




The question whether these reactions are direct substitutions or addition-elimination processes remains open because of lack of investigations specially devoted to this question.

## 7-1 FRIEDEL-CRAFTS REACTION*

The Friedel-Crafts reaction is applicable not only to the aromatic series, but to unsaturated compounds as well. The latter react with acid chlorides and with aluminium chloride to form unsaturated ketones.

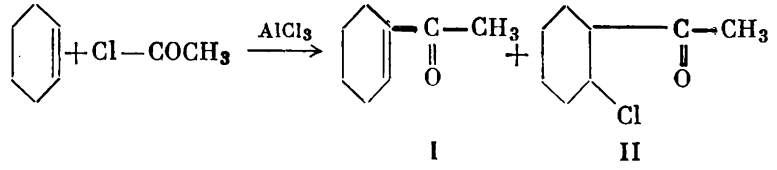
This reaction was first studied by Kondakov [12] for isobutylene and trimethylethylene (using zinc chloride instead of aluminium chloride).

The reaction between isobutylene and acetyl chloride resulted in mesityl oxide:

$$(CH_3)_2C=CH_2+ClCOCH_3 \xrightarrow{AlCl_3} (CH_3)_2C=CH-CO-CH_3+HCl$$

The reaction between cyclohexene and acetyl chloride has been the object of especially thorough study [13, 14].

If the reaction is accomplished in carbon disulphide with aluminium chloride the result is a mixture of two substances: tetrahydroacetophenone (I) and methyl-2-chlorocyclohexyl ketone (II)




I II

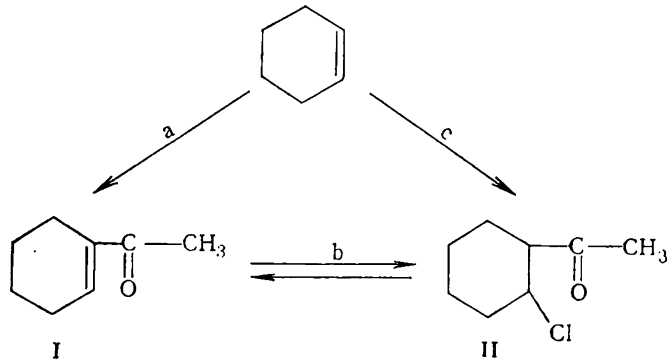
If heated for a long time with aluminium chloride the chloroketone eliminates hydrogen chloride and changes to the unsaturated ketone (I).

* See [10, 11] for review.

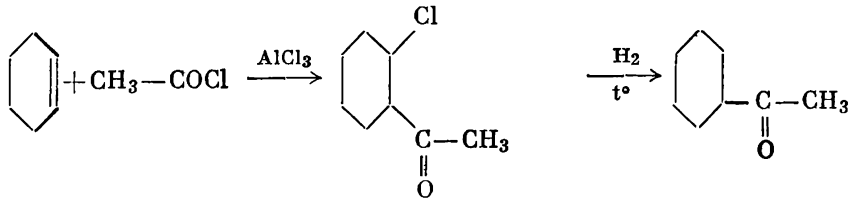
It has been suggested that the reaction under discussion proceeds so that only the chloroketone (II) forms from the cyclohexene at first, and then it splits off hydrogen chloride and changes into tetrahydroacetophenone (I).

However, this hypothesis has still to be proved, because as the elimination of hydrogen chloride from chloroketone (II) is a reversible reaction, it may be considered, conversely, that in the reaction between cyclohexene and acetyl chloride direct substitution takes place and only tetrahydroacetophenone (I) is formed, whereas the chloroketone is a by-product resulting from the addition of hydrogen chloride to the ketone (I).

The possible paths of the reaction (*a*, *b* or *c*, *b*) are shown in the scheme below




While studying this reaction Nenitzescu discovered the interesting reaction of *hydrogenating acetylation*. In the first stage at —10 to —15°, if two moles of $AlCl_3$ are added, the β-chloroketone results. Heating in the presence of cyclohexane (as the hydrogen donor) results in elimination of hydrogen chloride and the formation of a saturated ketone [15, 16]

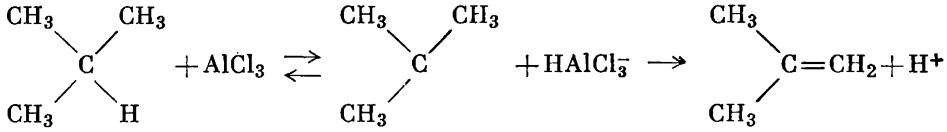



It was established further [17] that saturated compounds are also capable of the Friedel-Crafts reaction.

At first glance this fact contradicted the conclusion as to the analogousness of the Friedel-Crafts reaction for aromatic and unsaturated compounds.

However, detailed investigations by Nenitzescu and Hopff [19] established an important fact, namely, that aluminium chloride (especially anhydrous) acts as a dehydrogenator. As a result, unsaturated compounds are formed which enter into the Friedel-Crafts reaction.

The dehydrogenating action of aluminium chloride evidently consists in the aluminium chloride first tearing off a hydride ion and binding it into a complex. The resulting carbonium ion may split off a proton to form an olefin. The eliminated proton may combine with the complex-wise bound hydride ion; this may result in the liberation of elementary hydrogen or in the hydrogen acting as a hydrogenating agent.



$$H^+ + HAlCl_3^- \longrightarrow H_2 \text{ (or } 2H) + AlCl_3$$

The essential point in the Friedel-Crafts reaction with alkanes is the formation of alkenes. But the saturated compounds do not take part directly in the reaction.

Naturally, elucidation of the mechanism of the Friedel-Crafts reaction with saturated compounds does not in itself clear up the true course of the synthesis with unsaturated compounds.

It may finally be pointed out that the use of the Friedel-Crafts reaction in the unsaturated series opened out new interesting possibilities for synthesis. Syntheses of pyrylium salts [20] may serve as a characteristic example.

## 7-2 STEREOCHEMISTRY OF SUBSTITUTION REACTIONS AT THE ETHYLENE CARBON ATOM

The question of the mechanism of substitution at the olefinic carbon atom was studied for many years by Nesmeyanov and his collaborators.

Since many reactions formally considered substitution reactions are actually addition-elimination reactions, it was important to choose as objects of study such reactions wherein the double bond was not affected and where there was complete confidence that the process studied was one of direct substitution.

Such were the reactions of metal exchange in chlorovinyl organometallic compounds of the type

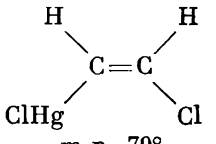
$$Cl-CH=CH-MeCl_{n-1}$$

Since these materials exist as *cis*- and *trans*-isomers, participation f the double bond in the reaction would be reflected in the configura- on of the reacting compound.

Nesmeyanov and coworkers studied the stereochemistry of these eactions.

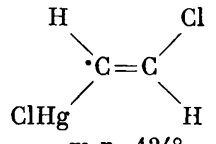
The two stereoisomers of β-chlorovinylmercuric chloride l — CH = CH — HgCl and the two stereoisomers of di-β-chloro- inyl mercury $(ClCH = CH)_2Hg$ were chosen as the initial mate- als; the configurations of all four compounds were determined y chemical and physical methods:

*cis*-Isomers

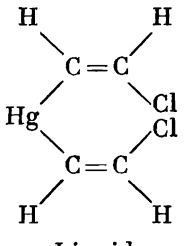


m.p. 79°

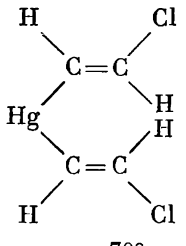
*trans*-Isomers



m.p. 124°



Liquid



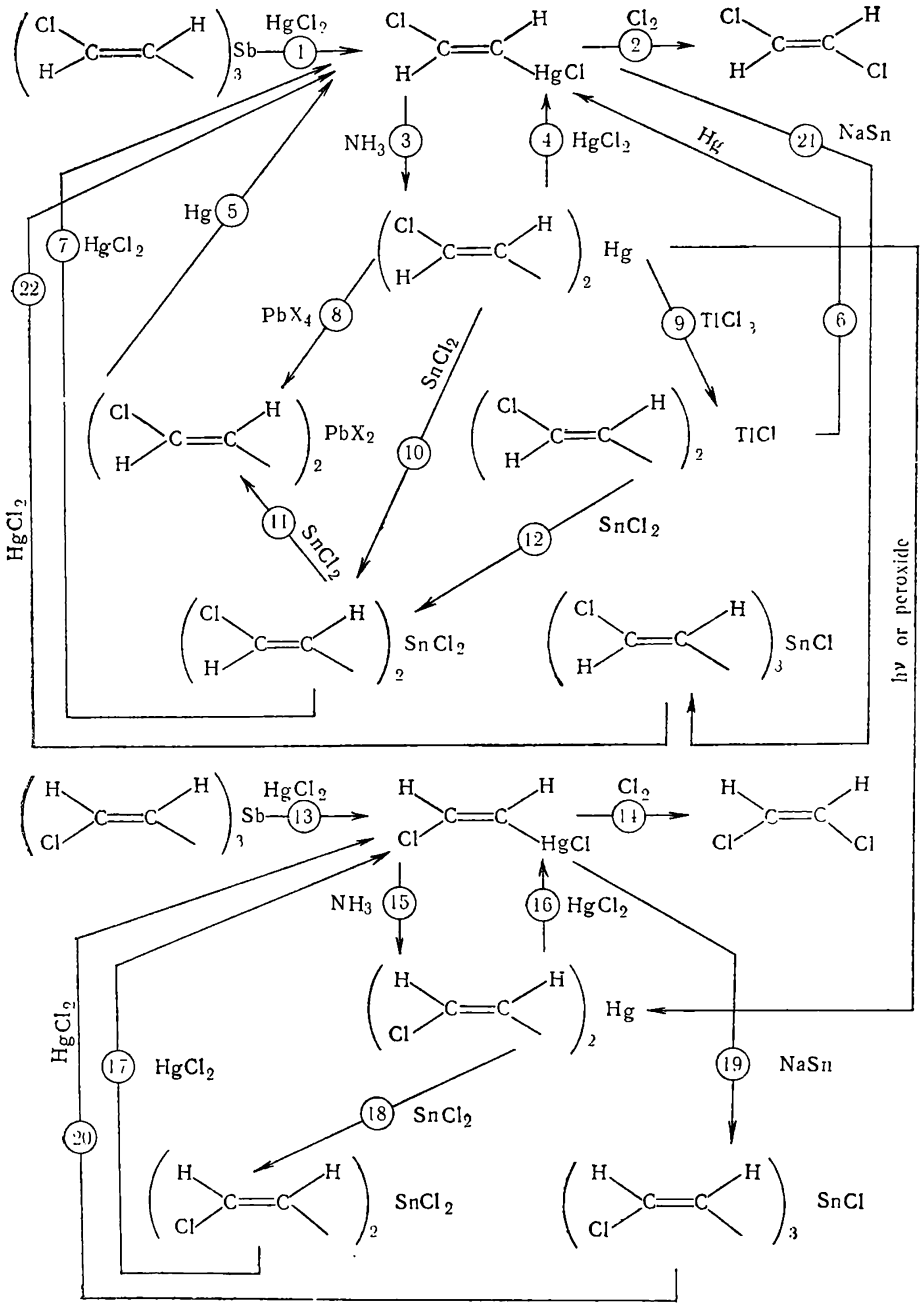
m.p. 70°

By reacting these four compounds one by one with chlorine, tannous chloride, thallium trichloride, lead tetraacetate, sodium- in alloy and metallic mercury, Nesmeyanov and Borisov carried ut a number of transfers of the chlorovinyl group from atom to atom nd traced the stereochemistry of these transfers [21].

In these exchange reactions only one stereoisomer of the new hlorovinyl compound was found to form in all cases. The configura- ion of the chlorovinyl group of the resulting stereoisomer was lways identical with the initial one.

The chlorovinyl group transfers studied are shown schematically n page 452.

Starting with *trans*-β-chlorovinylmercuric chloride, reaction cycles an be realized consisting of two, three or four steps and always eturning to the original *trans*-β-chlorovinylmercuric chloride (3,4) 3, 8, 5) (3, 9, 6) (3, 10, 7) (3, 8, 11, 7) (3, 9, 12, 7). It is hardly onceivable that in all these different reaction cycles the *trans*-con- guration of the chlorovinyl group changes to *cis*-configuration and ack exactly the number of times necessary in each case to bring back to the initial form.


HgCl2
Cl2
NaSn
Hg
NH3
HgCl2
HgCl2
Hg
PbX4
TlCl3
SnCl2
PbX2
TlCl
SnCl2
SnCl2
SnCl2
SnCl
hν or peroxide
HgCl2
HgCl2
NH3
HgCl2
Hg
HgCl2
NaSn
SnCl2
SnCl2
SnCl

Thus, all the reactions presented in the scheme take place with rict retention of the configuration of the chlorovinyl group when ansferred from atom to atom.

The exchange reactions shown in the scheme may be divided into wo groups. On the one hand, these are reactions of electrophilic ıbstitution at the unsaturated carbon atom:

$$(ClCH=CH)_2Hg + HgCl_2 \longrightarrow 2ClCH=CHHgCl$$
$$(ClCH)=CH)_2Hg + Pb(CH_3COO)_4 \longrightarrow$$
$$\longrightarrow (ClCH=CH)_2Pb(CH_3COO)_2 + Hg(CH_3COO)_2$$
$$(ClCH=CH)_2Hg + 2Cl_2 \longrightarrow 2ClCH=CHCl + HgCl_2$$
$$(ClCH=CH)_3Sb + 3HgCl_2 \longrightarrow 3ClCH=CHHgCl + SbCl_3$$
$$(ClCH=CH)_2SnCl_2 + 2HgCl_2 \longrightarrow ClCH=CHHgCl + SnCl_4$$

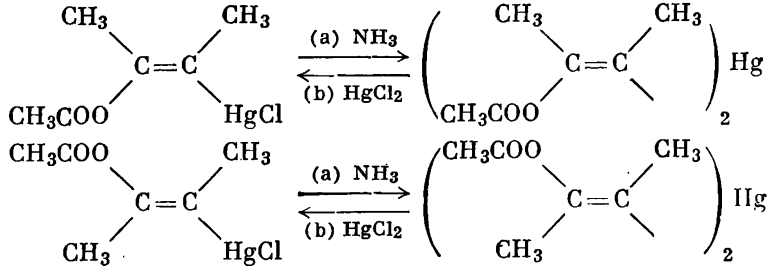
Electronically, these reactions are quite analogous to ordinary ıbstitution reactions in the aromatic series (halogenation, nitra- ion, mercuration, etc.).

On the other hand, some reactions undoubtedly follow a homolytic ıechanism:

$$(ClCH=CH)_2Hg + SnCl_2 \longrightarrow (ClCH=CH)_2SnCl_2 + Hg$$
$$(ClCH=CH)_2PbCl_2 + SnCl_2 \longrightarrow (ClCH=CH)_2SnCl_2 + PbCl_2$$
$$(ClCH=CH)_2PbCl_2 + 2Hg \longrightarrow 2ClCH=CH-HgCl + Pb$$
$$(ClCH=CH)_2TlCl + SnCl_2 \longrightarrow (ClCH=CH)_2SnCl_2 + TlCl$$

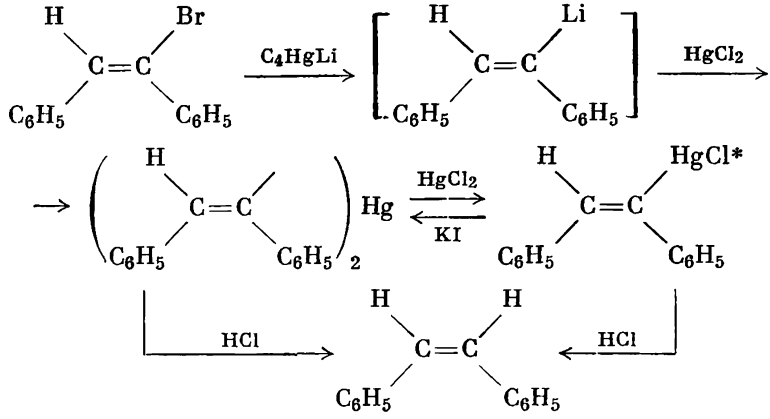
There is no reason to suppose that the chlorovinyl group is an xception.

Thus, the products of addition of mercuric acetate to dimethyla- etylene in the symmetrization reactions (a) and the desymmetriza- on reactions (b) also retain their configuration [22]:



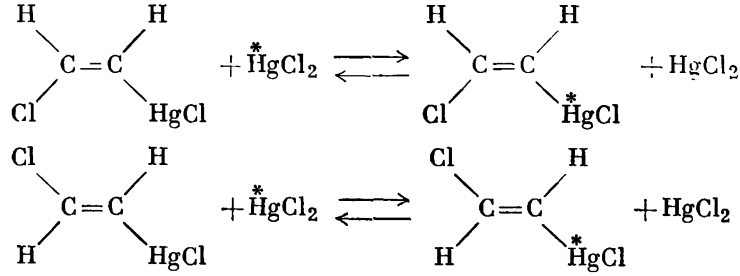

Exchange reactions of α-mercuriated derivatives of *cis*- and *trans*- ilbene synthesized from the corresponding α-bromo derivatives ırough organolithium compounds [23] also take place with reten-

tion of configuration.

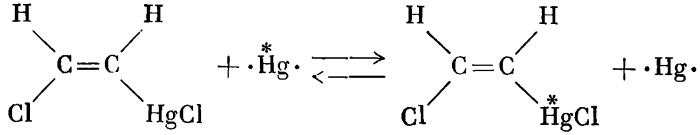


Direct proof of the retention of stereochemical configuration in reactions of homolytic and electrophilic substitution at the olefinic carbon atom was obtained by carrying out isotopic exchange reactions with the use of radioactive mercury $^{203}Hg$ [24].

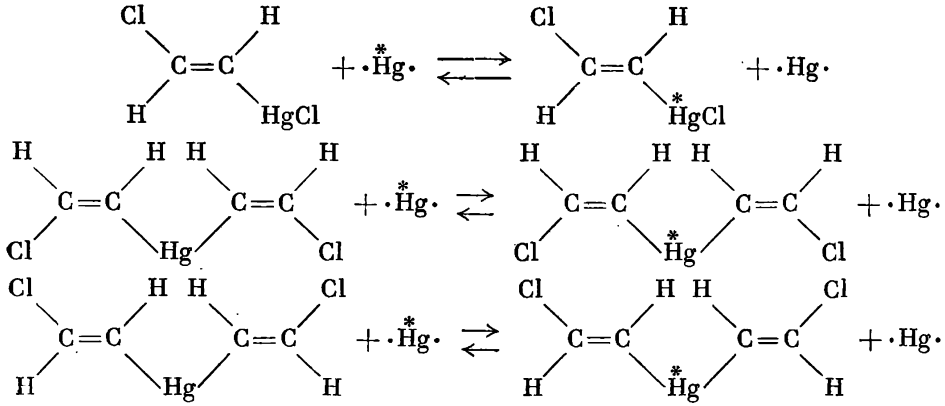
*Cis-* and *trans*-β-chlorovinylmercuric chlorides react rapidly in the cold in acetone with radioactive mercuric chloride with strict retention of configuration.



Similarly, *cis-* and *trans*-β-chlorovinylmercuric chlorides and bis-*cis-* and bis-*trans*-chlorovinyl mercury react with metallic mercury also with strict retention of geometric configuration:



[1] A similar cycle of reactions was carried out for the *trans*-series.

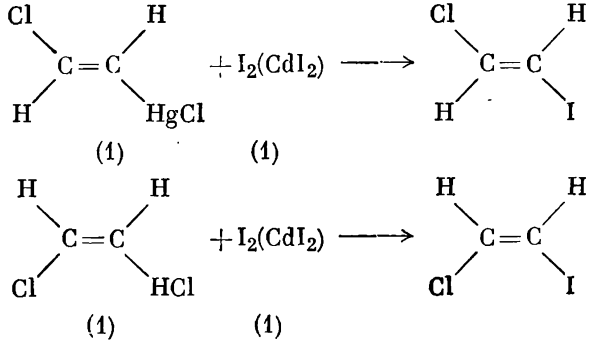


On the basis of the material given above Nesmeyanov and Borisov formulated the following general rule [25]: *Electrophilic and radical substitutions at the carbon-carbon double bond take place with retention of geometric configuration.*

The kinetics of the reactions under discussion was not studied until just recently, and so no sufficiently definite idea of their mechanism was available.

The kinetics of electrophilic substitution at the olefinic carbon was first studied for the interaction of *trans*- and *cis*-β-chlorovinylmercuric chlorides with iodine in the presence of cadmium iodide (in alcohol and acetone in the cold).

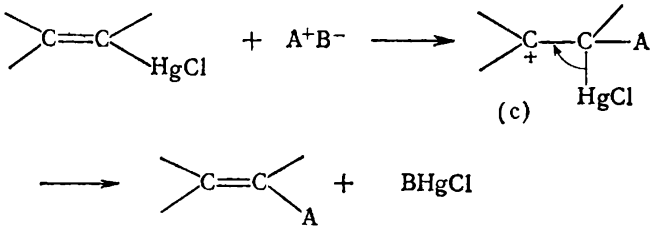
In both cases the reaction involves retention of geometrical configuration and is of a total second order (first order with respect to each of the components) [26].



Thus, these are reactions of bimolecular electrophilic substitution ($S_E 2$).

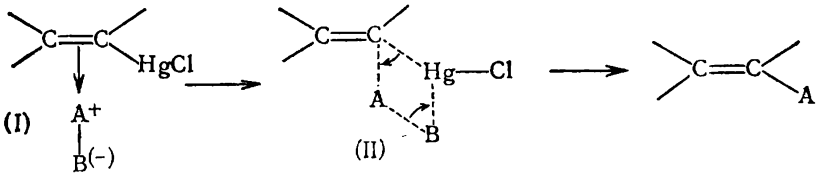
On the basis of the stereochemistry and kinetics of this type of electrophilic reactions an attempt may be made to outline their mechanism.

It may be stated that the reaction does not proceed in two steps with the formation of a carbonium ion:



If carbonium ion (c) were formed as an intermediate one would not expect the initial geometrical configuration to be retained.

It may be assumed that a π-complex (I) forms first, which then passes through the step of a cyclic intermediate state II, resulting in the final substance with retention of configuration.



Thus, bimolecular electrophilic substitution at the olefinic carbon atom involves retention of configuration, like $S_E2$ reactions at the saturated carbon atom.

In a strongly ionized solvent—dimethyl sulphoxide—the reaction of *cis*- and *trans*-β-chlorovinylmercuric chlorides with iodine is first-order with respect to the organomercury compound and zero-order with respect to iodine.

Apparently, the first, slow stage of the reaction is the formation of an ionic pair

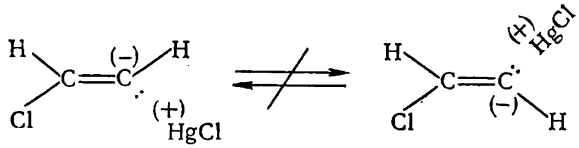
$$ClCH{=}CH{-}HgCl \xrightarrow[Slow]{DMSO} ClCH{=}CH^{(-)}\ {}^{(+)}HgCl$$

which then reacts quickly with iodine:

$$ClCH{=}CH^{(-)}\ {}^{(+)}HgCl \xrightarrow[Fast]{I_2} ClCH{=}CH{-}I$$

It is especially interesting that the reaction involves retention

f configuration.* From this it follows that the free electron pair xes geometrical configuration (under conditions of an ionic air)



In concluding, special mention should be made of reactions f homolytic substitution at the olefinic carbon atom.

Obviously, as a matter of principle, reactions of this type may e both free-radical and reactions during which no radicals form s kinetically independent particles.

There is no doubt that the homolytic isotope exchange reactions iven above, which take place under very mild conditions, are not ree-radical reactions. Nor have we any grounds to be certain that here was even a single free-radical reaction among the homolytic nes studied by Nesmeyanov and Borisov.

The photochemical reaction (scattered sunlight) of *trans-* and *s*-β-chlorovinylmercuric chlorides with iodine in carbon tetrachlo- de in the cold was employed as the object for studying the kinetics nd stereochemistry of free-radical substitution.

The reaction is first-order with respect to iodine and zero-order ith respect to the organomercury compound. This free-radical eaction results in the same isomer mixture (50% *trans-* and 50% *s*-isomers) of chloroiodoethylenes, irrespective of whether the

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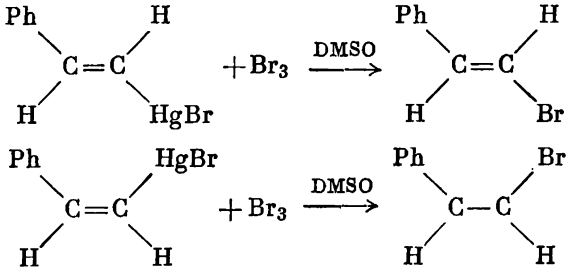
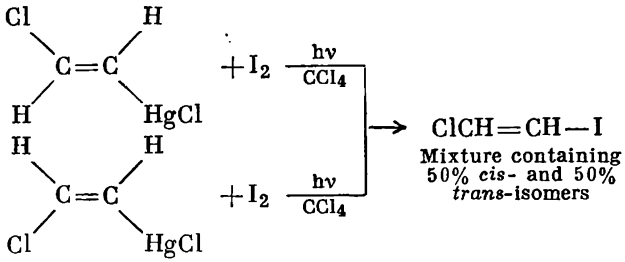
* Quite a similar result was obtained in the reaction between ω-bromo- ercurstyrene and bromine:



n both cases the reaction is kinetically first-order with respect to the organo- ercury compound, zero-order with respect to bromine and involves retention geometrical configuration.

*trans*- or the *cis*-organomercury compound is used.




It was established by means of duplicate tests that no secondary isomerization of *cis-trans*-chloroiodoethylenes is superimposed on this result.*

Thus, the rule for homolytic substitution at the olefinic carbon atom can be formulated the most accurately as follows: *homolytic reactions of substitution at the olefinic carbon atom not involving the formation of radicals as kinetically independent particles proceed with retention of geometrical configuration; reactions of free-radical substitution do not involve retention of configuration.*

Nucleophilic substitution at the olefinic carbon atom is the most obscure with respect to stereochemistry. Though several papers have been published on this question [27], no definite regularities can as yet be indicated.

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* If left standing in the light for a long time both *cis*-chloroiodoethylene and *trans*-chloroiodoethylene change into the same equilibrium isomer mixture containing 17.5% of *cis*-chloroiodoethylene and 82.5% of *trans*-chloroiodoethylene. In the experiments under discussion, however, the mixture of chloroiodoethylenes that formed was approximately equimolecular.

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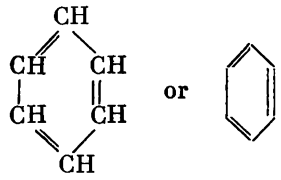
# 8

# AROMATIC SUBSTITUTION

## 8-1 STRUCTURE OF BENZENE

The aromatic series consists of compounds containing a special cyclic grouping of six carbon atoms; the simplest grouping of this kind is that of benzene.

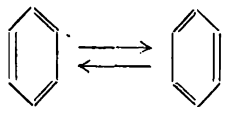
The benzene molecule is a ring composed of six methenyl groups. The structure of benzene is generally represented by Kekulé's formula:




It should be kept in mind that this formula, while giving the correct sequence of atomic bonds in the benzene molecule, is unsatisfactory in a number of respects.

According to this formula, a benzene molecule should have an axis of symmetry of the third order and the shape of an irregular hexagon, because the length of the single C — C bond is generally equal to 1.54Å, while the length of the double bond is 1.32Å. Actually, the benzene molecule has an axis symmetry of the sixth order and all six carbon-carbon bonds have the same length 1.40Å, intermediate between the lengths of the single and the double carbon-carbon bond.

Attempts to coordinate Kekulé's formula with experimental data by assuming extremely rapid oscillation of bonds (electronic tautomerism) are devoid of physical basis.



Data available at present indicate the following structure of benzene: all six carbon (and six hydrogen) atoms are in the same plane (experimental fact) and the orbitals of π electrons of the carbon atoms are perpendicular to the plane of the molecule (and therefore parallel to each other).

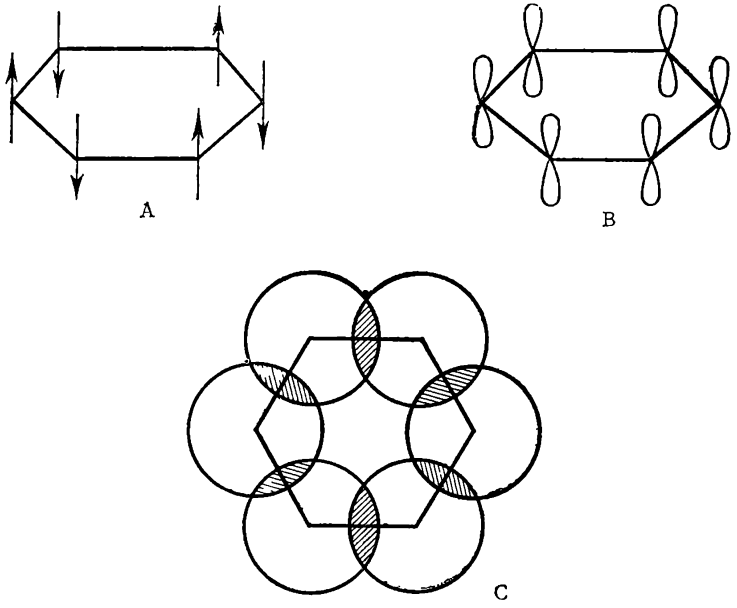
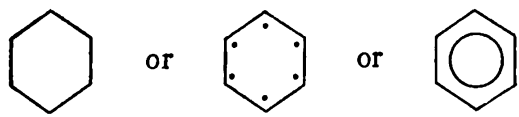



FIGURE 8-1 Electronic cloud of benzene ring

In Fig. 8-1A the π electrons are designated by arrows. The different directions of the arrows show that the π electrons of neighbouring carbon atoms have different spins. The orbital of each π electron is overlapped by the orbitals of both its neighbours. This peculiarity of the π orbital of the benzene ring is not reflected in Fig. 8-1A or B, but becomes evident if the three-dimensional electronic model of the benzene molecule (of the model type pictured in Fig. 8-1B) is projected on a plane (Fig. 8-1C).

Thus, each carbon atom of the benzene ring is linked to its two neighbouring atoms not only with σ but also with π electrons.

It would be logical to picture the benzene formula as:

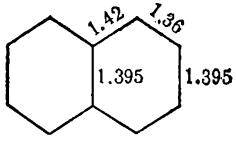


(Dots in the second formula and inner ring in the third symbolize a sextet of π electrons.) However, in order to preserve the usual concepts of quadrivalence of carbon, chemists use Kekulé's formula while clearly realizing its virtues and shortcomings.

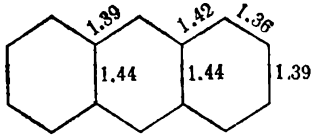
The carbon-carbon bond in benzene differs from the ethylene bond in electron density and length. In ethylene the double bond is a combination of a σ bond and a π bond formed by two π electrons. In benzene, besides the σ electrons, there is an electron density for each C — C bond equal to the density of one π electron.

In condensed aromatic hydrocarbons the electron density of some C — C bonds is still smaller. In graphite the electron density of each C — C bond is equal to the density of two σ electrons and 2/3 π electron.

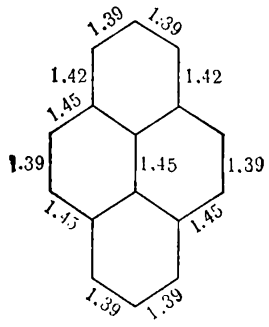
In the benzene ring all the interatomic distances are equal (1.40Å), however in more complex aromatic hydrocarbons they are not equal. Interatomic distances in naphthalene, anthracene, pyrene and coronene are given below [1, 2].



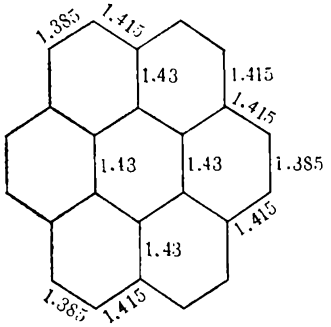

Naphthalene




Anthracene



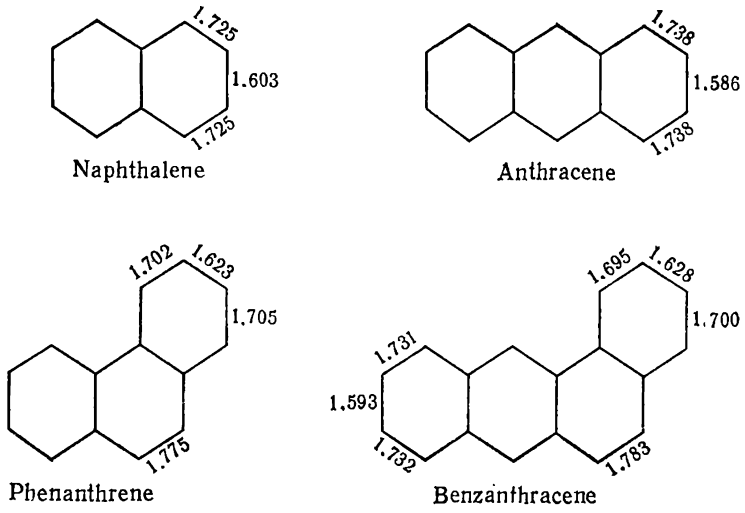

Pyrene




Coronene

The concept of "bond order" or "bond factor" is often used to characterize individual bonds in aromatic compounds. If the "bond factor" of the C — C bond in ethane is taken as 1 and of the C=C bond in ethylene as 2, then the bond factor in aromatic hydrocarbons

will usually lie between 1 and 2.




Bond factors depend on their length and electron density. Thus, of two bonds with the same electron density the one that is shorter will have the larger bond factor.

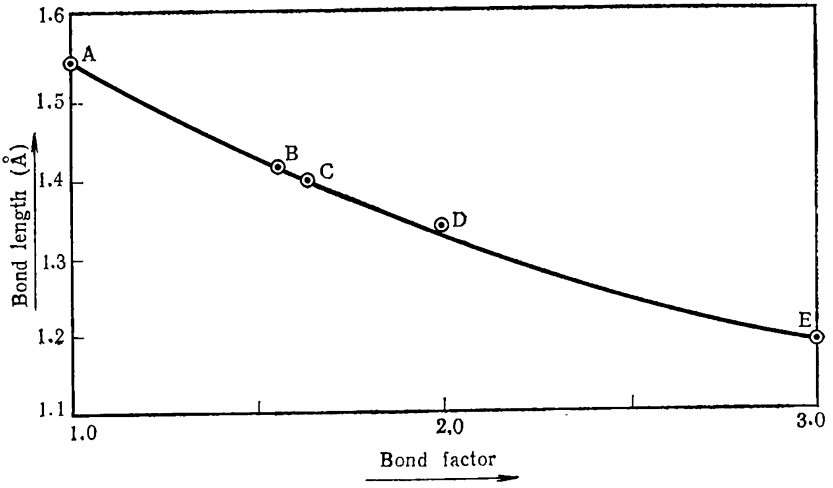



FIGURE 8-2 Dependence of bond lengths on bond factor

If the length of the bond is determined experimentally, its bond factor can be calculated; and conversely, if the bond factor is known, the bond length can be calculated.

Above are given the values of the bond factors in some hydrocarbons calculated according to the molecular orbitals method [3].

For benzene the order of all bonds, calculated by this method is 1.667, for graphite—1.53.

The dependence between bond lengths and bond factors (calculated by the method of molecular orbitals) is represented in Fig. 8-2, where points are given for ethene (*A*), graphite (*B*), benzene (*C*), ethylene (*D*), and acetylene (*E*).

## 8-2 THE CONCEPT OF AROMATICITY

In organic chemistry there exists the concept of *aromaticity* or *aromatic properties*. By aromaticity chemists understand the ability of a substance to take part readily in substitution (but not addition) reactions and stability toward oxidizing agents. This concept originated as a result of studies of benzene which, contrary to ethylene hydrocarbons, in spite of its formal unsaturation, participates readily in substitution reactions, and is stable toward oxidizing agents. Later it was found that aromatic hydrocarbons feature high thermodynamic stability as well.

It should be kept in mind that difficulties are apt to arise when the concept of aromaticity is applied to different compounds. A substance is considered the more aromatic the easier it enters into a substitution reaction and the more difficult it is to oxidize. However, the changes in these properties on passing from substance to substance are often not consistent.

If benzene is compared with, say, ethylene, the lack of aromatic properties in the latter compound is quite obvious: ethylene readily undergoes addition (but not substitution) reactions and is easily oxidized. But if we compare benzene with naphthalene, difficulties begin to arise: naphthalene enters into substitution reactions more readily but also oxidizes more readily. A similar situation comes up if we compare the aromaticity of benzene and pyrrole. The latter, as it is sometimes said, possesses "superaromatic properties" (enters very readily into substitution reactions), however, it also is readily oxidized.

It follows from the above discussion that the concept of aromaticity has a relative meaning; apparently, it is more useful to apply it for comparing aromatic compounds with other classes of substances, than aromatic substances with each other.

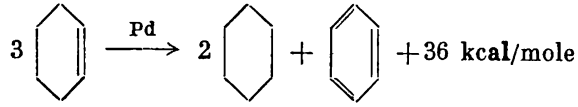
## 8-2.1 Non-benzenoid Aromatic Systems

### Aromatic Compounds not Containing Benzene Rings, but Having a "Benzenoid" Electronic Configuration

The benzene ring is thermodynamically stable. This follows, for instance, from the abnormally low heat of hydrogenation of benzene to cyclohexadiene.

Whereas the heat of hydrogenation of cyclohexene to cyclohexane is 23.5 kcal/mole, and that of cyclohexadiene to cyclohexane 28.5 kcal/mole, the hydrogenation of benzene to cyclohexadiene, disrupting the stable aromatic system, produces only 4.5 kcal/mole.

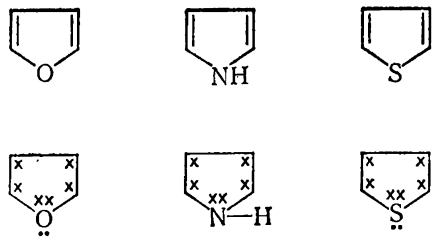
The same reason is given for the ease of the irreversible catalysis of Zelinsky [4], the catalytic conversion of three cyclohexene molecules into two molecules of cyclohexane and one molecule of benzene:




Owing to the thermodynamic stability of benzene and other aromatic hydrocarbons, they form easily in various pyrogenetic processes.

If in a cyclic system there are two conjugated double bonds and if, besides, there is a possibility of an additional double bond arising to form a cyclic system of six electrons ("benzenoid electron system"), this possibility is generally easily realized, as in the case of dehydrogenation of cyclohexadiene. The part of the fifth and sixth $\pi$ electrons, however, may often be played by a free pair of $p$ electrons of a heteroatom (oxygen, nitrogen, sulphur, and others) suitably positioned in the ring.

Such is the situation, for example, in the simplest five-membered heterocycles — furan, pyrrole and thiophene.




Since the formation of a closed system of six electrons ("benzenoid" system) is energetically advantageous, the role of the lacking

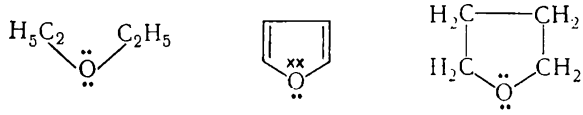
to make six) $\pi$ electron pair in these compounds is played by the unshared $p$ electrons (designated by crosses) of oxygen, nitrogen and sulphur.

Evidently, the electronic configuration of these five-membered heterocyclic rings is like electronic configuration of the benzene ring. This is responsible for the aromatic properties of the benzene ring.

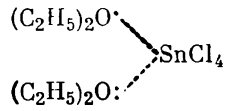
If the $p$ electrons of the heteroatoms did not interact with the $\pi$ electrons of the double bonds, these heterocyclic compounds would be close in chemical nature to butadiene rather than to aromatic hydrocarbons.

Naturally, the participation of the $p$ electrons of heteroatoms in the formation of the cyclic electronic configuration cannot but affect the chemical nature of these heteroatoms.

For example, the oxygen in furan differs from the oxygen in an ether or in tetrahydrofuran:



The oxygen of ether and of tetrahydrofuran readily forms an oxonium-type compound, for example, with $SnCl_4$:



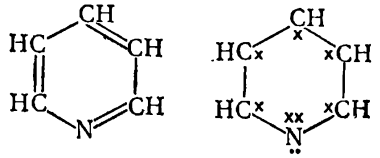
The oxygen of furan, whose $p$ electrons interact with the $\pi$ electrons of the ring (as the result of which oxygen carries a positive charge and is of an oxonium nature), forms no complex with $SnCl_4$.

The participation of the $p$ electrons of nitrogen in the interaction with the $\pi$ electrons of the ring results largely in the nitrogen of pyrrole losing its basic properties, so characteristic of secondary amines. The sulphur of thiophene is not at all like the sulphur in thioethers, being stable, for example, to the action of oxidizing agents.

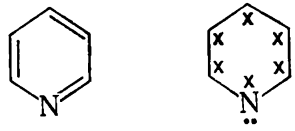
The importance of the "benzenoid" electronic configuration for aromatic properties is apparent from the fact that heterocycles, little or not at all resembling benzene in composition and structure, but having a closed system of six electrons, possess aromatic properties.

Such, for example, is pyridine, which is stable to oxidizing agents and participates in substitution reactions (with greater difficulty

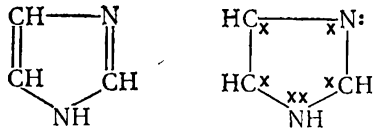
than benzene).



As the two electrons of the nitrogen atom do not participate in the formation of the "benzenoid" electronic system, pyridine is a base:

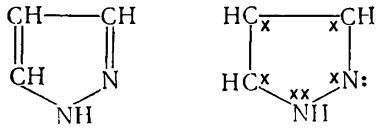


Imidazole possesses aromatic properties (participates in substitution reactions, is stable toward oxidizing agents — is not affected by $H_2Cr_2O_7$, but is decomposed by $KMnO_4$).



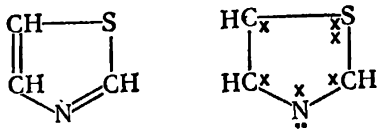
As the *p* electron pair of one of the nitrogens does not participate in the formation of the "benzenoid" electron system, imidazole, unlike pyrrole, possesses basic properties.

Pyrazole has still more pronounced aromatic properties:

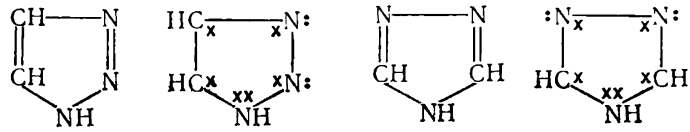


Pyrazole can be halogenated, nitrated, sulphonated; its amino derivatives can be diazotized. Pyrazole is just as resistant to oxidizing agents as benzene.

Thiazole possesses aromatic properties resembling those of pyridine.



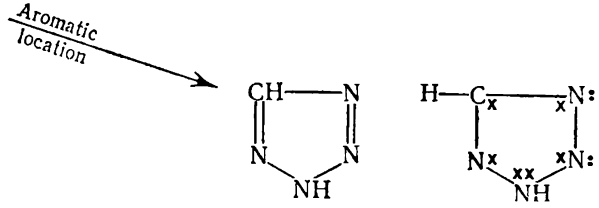
The triazoles



1,2,3 – Triazole 1,2,4 – Triazole

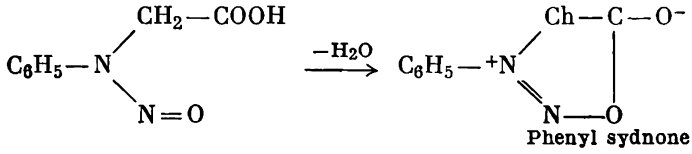
have only two methenyl groups; nevertheless triazoles are stable compounds of an aromatic nature.

In tetrazole

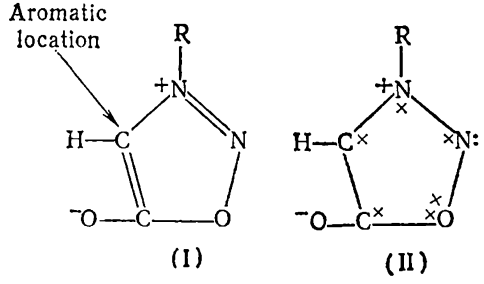



there is only one methenyl group; however, it also exhibits aromatic properties. Tetrazole is stable, it enters into substitution reactions: its amino derivatives diazotize.

Analogously sydnone* molecules, which can be obtained by eliminating water from *N*-nitrosoamino acids, e.g.,




have only one methenyl group in a five-membered ring, and nevertheless, the sydnone system possesses aromatic properties [3].




The electronic system of sydnones consists of 6 π electrons as is indicated in formula (II).

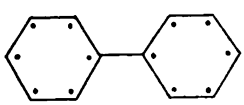
* These compounds were called sydnones, because they were first synthesized and studied at the University of Sydney.

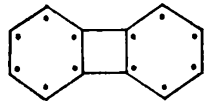
Sydnones are halogenated and nitrated at the CH. There have been no other reports of electrophilic substitutions (such as sulphonation and acylation), however very few attempts have been made in this direction.

## 8-2.2 Conditions of Aromaticity of Molecules

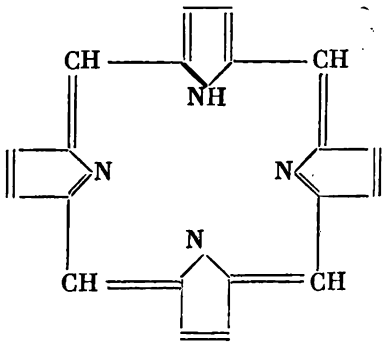
Aromatic compounds do not necessarily need to have a cyclic sextet of $\pi$ electrons. Thus, condensed hydrocarbons—naphthalene, anthracene, phenanthrene—have more complex cyclic $\pi$ electron systems, but possess aromatic properties.

Biphenyl and biphenylene have continuous systems of 12 $\pi$ electrons and are aromatic compounds:

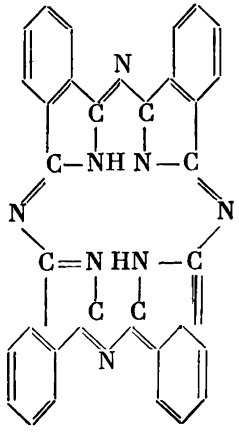




It follows from the above discussion that a characteristic indication of the structure of compounds of aromatic nature is the presence of a closed system of $\pi$ electrons (closed system of conjugated bonds). This closed system of conjugated bonds may be quite complex and nevertheless the molecule will be aromatic in character. For example, the aromatic ring of porphyrine and phthalocyanine consists of 16 atoms:



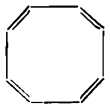

Porphyrine system




Phthalocyanine

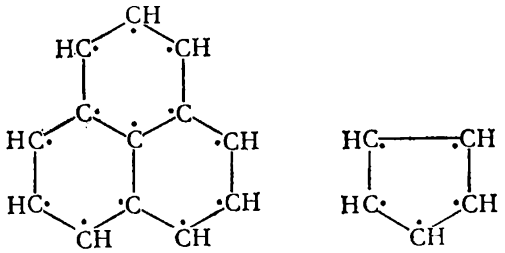
One of the most important conditions of aromaticity of a molecule is its *coplanarity*. The cyclooctatetraene molecule contains a closed system of four conjugated double bonds, but is not planar in structure (coplanarity of cyclooctatetraene is impossible owing to

great Baeyer strain):

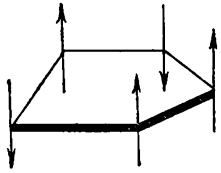


In cyclooctatetraene the axes of all the electron clouds cannot be placed parallel to each other so as to form a uniform electron system when they overlap, such as that in benzene (page 461). Therefore cyclooctatetraene is a system of closed but isolated double bonds. Hence the typically unsaturated properties and complete lack of aromatic properties in cyclooctatetraene.

Another important condition of an aromatic molecule is pairing of all its $\pi$ electrons forming the closed system. To be aromatic it is insufficient for a molecule to have a cyclic closed system of electrons. Two molecules are shown below, where these conditions are satisfied and yet they are not capable of existence:



This inability to exist is due to both systems having an odd number of $\pi$ electrons, as a result of which one of the electrons is not paired. This is clearly illustrated by the example of cyclopentamethine (the arrows indicate $\pi$-electron spins):



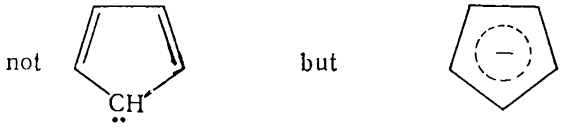
Since two electrons with the same spin repel each other, this system is unstable. Both systems are free radicals.

Hence, a $\pi$-electron system of aromatic compounds may have only an even number of electrons.

The cyclopentadienyl radical forms a compound of aromatic character with metallic iron—dicyclopentadienyl iron (ferrocene), but in it all the $\pi$ electrons are paired (see page 34).

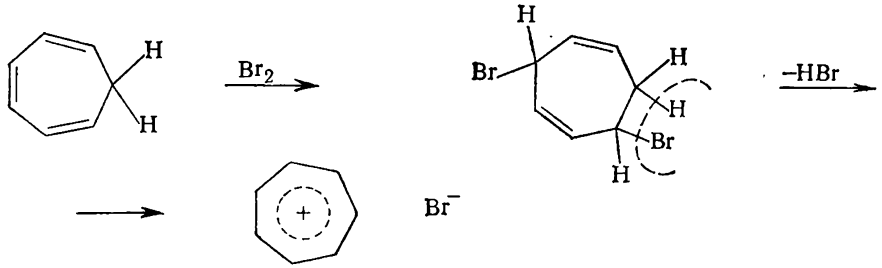
When one electron adds to the cyclopentadienyl radical, a cyclopentadiene ion possessing aromatic character is formed. The sixth $\pi$

electron is not localized at any one carbon atom but is shared equally by all five carbon atoms of the ring:




The equivalence of all the CH-groups of cyclopentadienyl ion was demonstrated by Kursanov and coworkers [6] and also by X-ray investigations of $(C_5H_5)_2Mg$ [7] and $(C_5H_5)_2Mn$ [8].

Tropylium ion [9], prepared in 1954, is also of an aromatic nature:

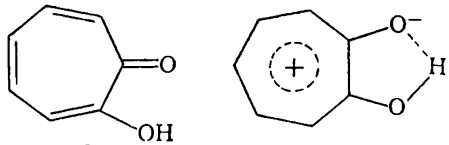



Tropylium cation

It is interesting to note that Hückel predicted as far back as 1931 [10] that cyclopentadienyl anion and tropylium cation would be aromatic in nature, basing his conclusions on molecular orbital calculations.

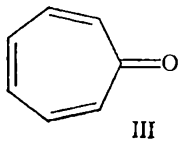
Hückel derived a general rule according to which *monocyclic conjugated polyenes possessing the symmetry of a regular polygon have a closed electron shell and consequently aromatic stability if the number of* $\pi$ *electrons equals* $4n + 2$ (*where n is an integer*).

Only fourteen years later Hückel's idea of the possibility of existence of a stable seven-membered aromatic system was successfully employed [11] to elucidate the structure of a new class of natural substances—tropolones, because the properties of tropolones differed considerably from those expected of a substance with structure I. The postulate that the molecule is based on a seven-membered aromatic cation (structure II) eliminated the inconsistencies between the properties and the structure of these substances.

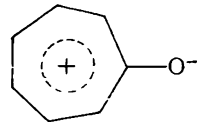



I II

The structure of tropolone is also better expressed by formula IV than by formula III.




III




IV

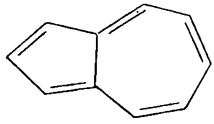
Thropolone, like other ionic compounds, is miscible with water. Its boiling point (113°/15 mm) is much higher than that of the isomeric benzaldehyde (68°/15 mm).

However, the separation of charges in the tropolone molecule is apparently not complete (as required by formula IV). This is evident from the value of the dipole moment of tropolone—4.3 D (the dipole moment of benzophenone is 2.97 D and that of acetone 2.8 D). If the separation of charges were complete, the dipole moment should have been larger.

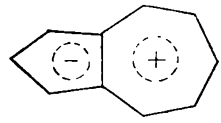
The true structure of tropolone is evidently intermediate between structures III and IV.

A very interesting class of non-benzenoid aromatic compounds are the *azulenes* whose molecules comprise a condensed system of five- and seven-membered rings.*

Structural formula V was the first one proposed for these blue or violet hydrocarbons.



V




VI

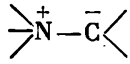
However the presence of a dipole moment (1.09 D) indicates that the structure of the azulene molecule is closer to the bipolar formula VI [13]. Quantum mechanical calculations confirm this conclusion [14].

Thus, all the carbon atoms of the five-membered ring carry a negative, and all the carbon atoms of the seven-membered ring (exclusive of the two common carbon atoms) a positive charge. Such a separation of charges (though apparently incomplete) is an important reason for the stability of both rings.

An interesting example of mutual stabilization of oppositely charged nuclei are certain *ylides*, substances with a semipolar bond

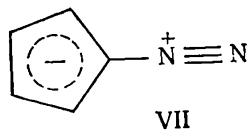
* For reviews on azulenes see [12].

›etween a carbon atom and the adjacent nitrogen atom (or other ›nium atom) [15].



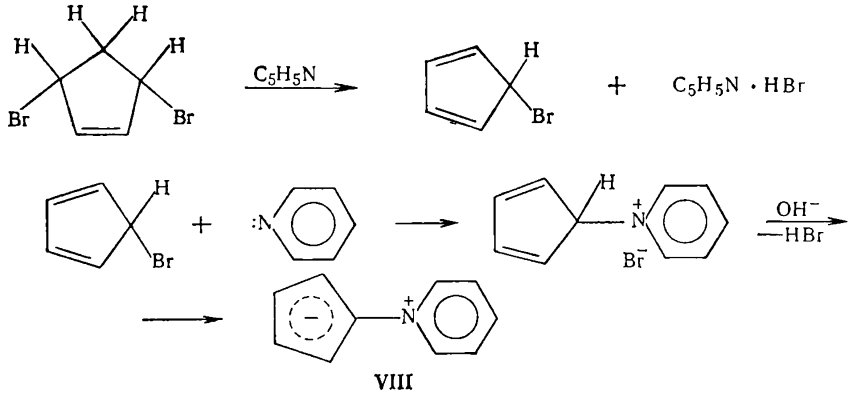
Generally ylides are highly unstable compounds, and their ›xistence is surmised by the products of their transforma- ;ions.

However, if an ylide carbon atom is one of the atoms of a cyclopen- ;adienyl system, the ylide is capable of existence, e.g., diazocyclo- ›entadienylide (VII) [16].



VII

Pyridine cyclopentadienylide (VIII) is particularly stable. ;t can be obtained by treating pyridine with dibromocyclopentene ;ollowed by treatment with caustic [17].



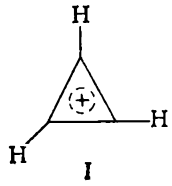
VIII

## 3-2.3 Three-Membered Aromatic Compounds

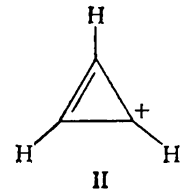
According to Hückel's rule, a cyclic conjugated system will possess aromatic stability if the number of $\pi$ electrons equals $4n + 2$, where $n = 0, 1, 2, 3$ or any other integer.

Consequently the simplest aromatic system ($n = 0$) should have only two $\pi$ electrons. The structure of such a system should be described better by formula I than by formula II.

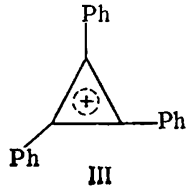
Recently many stable derivatives of this system [18] have been synthesized, e.g., III.



I

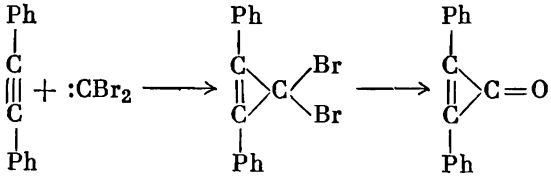


II



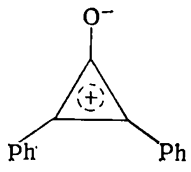
III

Of interest among the compounds of this class is diphenylcyclopropenone (IV), prepared from dibromocarbene and diphenylacetylene followed by hydrolysis [19].

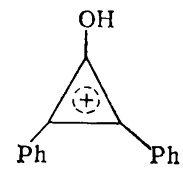


IV

The high dipole moment (5.08 D) indicates that the true structure of diphenylcyclopropenone is intermediate between structures represented by formulas V and VI.



V



VI

iphenylcyclopropenone forms salts with hydrogen halides, the structure of which corresponds to formula VI.

## 8-3 SUBSTITUTION IN THE BENZENE RING

Substitution reactions in the benzene ring are practically the most important and the most widely studied of substitution reactions of aromatic hydrocarbons. General principles discovered in the

chemistry of benzene have been applied successfully in many cases to other areas of organic chemistry.

In substitution reactions in the nucleus of benzene derivatives the new substituent enters predominantly into definite positions with relation to already existing substituents. This phenomenon is called orientation. The point of entry of the new substituent depends on the nature of the substituent already present (if there are several—on the nature and relative position of them all), on the nature of the new substituent, on the nature of the acting reagent and on the reaction conditions (temperature, catalysts, solvent, etc.).

For the practically most important substitution reactions in the benzene ring, viz., halogenation, nitration, sulphonation, condensation with oxygen compounds (aldehydes, ketones, alcohols) there are two basic types of orientation of the entering substituent with respect to the one already present: *ortho-para-* and *meta*-orientation. In this connection one generally distinguishes between substituents (or orientants) of the 1st kind, which direct the new substituent predominantly into the *ortho-* and *para*-positions and substituents of the 2nd kind which direct it predominantly into the *meta*-position. Orientants of the 1st kind activate the benzene ring, as a rule, while orientants of the 2nd kind passivate it with regard to substitution reactions.

Orientants of the first kind include:

$$OH,\ OR,\ OCOR,\ SH,\ SR,\ NH_2,\ NHR,\ NR_2,\ NHCOR,\ -N{=}N-,\ CH_3,$$
$$CH_2R,\ CHR_2,\ CR_3,\ CH_2Cl,\ CH_2OH,\ CH_2ONO_2,\ CH_2NH_2,\ CH_2CN,$$
$$CH_2COOH,\ CH_2CH_2COOH,\ CH{=}CH-COOH,\ CH{=}CH-NO_2,$$
$$\overset{+}{C}H_2\overset{+}{A}sR_3,\ C_6H_5,\ F,\ Cl,\ Br,\ I^*$$

Orientants of the second kind include:

$$SO_3H,\ NO_2,\ COOH,\ COOR,\ CONH_2,\ COCl,\ COR,\ COCOOH,\ C(OH)Ar_2,\ CN,$$
$$CCl_3,\ CF_3,\ \overset{+}{N}H_3,\ \overset{+}{N}H_2R,\ \overset{+}{N}HR_2,\ \overset{+}{N}R_3,\ \overset{+}{P}R_3,\ \overset{+}{A}sR_3,\ \overset{+}{S}bR_3,\ \overset{+}{S}R_2,$$
$$\overset{+}{I}Ar,\ CH_2\overset{+}{N}R_3,\ POR_2,\ B(OH)_2,\ CHO$$

Naturally, there are also atomic groupings of intermediate nature, causing mixed orientation. Among these are:

$$NO,\ COCH_3,\ CH_2F,\ CHCl_2,\ CH_2NO_2,\ CH_2CH_2NO_2,\ C(CH_2)_2NO_2,$$
$$CH_2CH_2\overset{+}{N}R_3,\ CH_2\overset{+}{P}R_3,\ CH_2\overset{+}{S}R_2 \text{ and others}$$

The nature of orientation of the above groupings remains the same for the naphthalene, anthracene, etc., rings as well, but the substi-

* Unlike other substituents of the 1st kind, halogens passivate the benzene ring with regard to substitution reactions.

tution rules naturally become more complex due to the possibility of reactions taking place in different nuclei and to the inequality of the carbon atoms in the unsubstituted hydrocarbons.

For a long time the phenomenon of orientation was studied only qualitatively.

A new stage in the study of this phenomenon began with the works of Holleman [20] who indicated the role of the kinetic factor. He showed that the position of the entering substituent is determined by the relative rates of three simultaneous competing substitution reactions: in the *o*-, *m*- and *p*-positions. Substitution in the *o*- and *p*-position always takes place faster than substitution in *m*-position. Therefore in the case of uncoordinated orientation of two substituents the point of entry of the third substituent into a benzene ring is generally determined by the influence of the *ortho-para* directing orientant. If both substituents are orientants of the same kind, the predominant direction of substitution is determined by the one with the stronger influence (Beilstein's rule).

Holleman developed relative power-of-orientation series for *ortho-para*- and *meta*-orientants on the basis of a study of substitution reactions of *para*-disubstituted benzenes. For example, *p*-chlorotoluene nitrates primarily in *ortho*-position with respect to the chlorine atom. This suggests that chlorine is a stronger *ortho-para* orientant than methyl.

On the basis of such experimental material the following orientation power series (Holleman series) were developed:

For *ortho-para* substituents: $OH > NH_2 >$ halogens $> CH_3$.

For *meta* substituents: $COOH > SO_3H > NO_2$.

Holleman's subsequent kinetic investigations confirmed his rules in general. However, as analyses of isomer mixtures became more accurate, it was established that cases of 100 % *ortho-para*-orientation or 100 % *meta*-orientation are rather rare. Usually a mixture of all three isomers forms with *o*- and *p*-isomers or *m*-isomers predominating, depending on whether the substituents already present are of the 1st or 2nd kind, respectively.

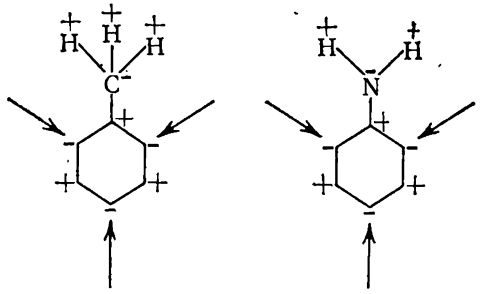
Thus, it became apparent that the rules of orientation, discovered empirically, are but approximations.

## 8-3.1 Theory of Substitution in the Benzene Ring

At the beginning of this century a number of attempts were made to explain orientation in the benzene ring, proceeding from concepts of alternating polarity (Frey, Vorländer, Berkenheim and others).

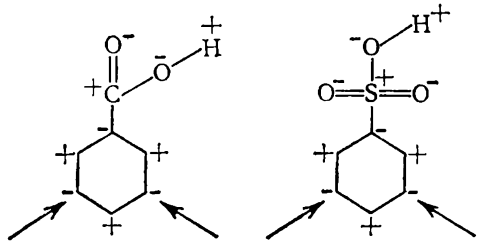
According to these concepts the carbon atoms of the benzene ring in benzene derivatives are alternately positively and negatively charged. This alternate polarity is caused by the substituents.

If the benzene ring contains *ortho-para* orientants, say, $CH_3$ or $NH_2$,



ıe *o*- and *p*-carbon atoms are negatively charged. Electrophilic substitution, .z., exchange of hydrogens for $NO_2$, $Cl^+$, $^+SO_3H$, etc., will occur predominantly ı these positions.

If, however, the benzene ring contains *meta*-directing substituents the negave charges will be carried by the *m*-carbon atoms:



In these cases electrophilic substitution will naturally occur readily in the *eta*-position.

Thus, alternating polarity concepts make it possible to explain why substiıents of the 1st kind orient in the *o*- and *p*-, and substituents of the 2nd kind, the *m*-position. However, these concepts cannot account for the fact that ·ientants of the 1st kind facilitate electrophilic substitution reactions while ·ientants of the 2nd kind impede them.

The majority of substitution reactions in the benzene ring are ractically irreversible. An example of a reversible reaction is ılphonation: under the influence of a sulphonating mixture some the sulpho-acid isomers may be transformed into others. In most ther substitution reactions no mutual transformations of *o*-, *m*- nd *p*-isomers are observed. For this reason the relative yields of -, *m*- and *p*-isomers are determined by the relative rates of *o*-, *m*- nd *p*-substitution (kinetic factor) rather than by the change in ıe free energy in *o*-, *m*- and *p*-substitution (thermodynamic factor).

As was indicated earlier (page 102) the basic approximate rate ıuation of chemical reactions is:

$$k = PZe^{-\frac{E}{RT}}$$

In the general case, the product $PZ$ may be different for the *o*-, *m*- and *p*-substitutions. As monosubstituted benzene has two *ortho*-, two *meta*- and one *para*-position, it would seem that the probabilities of reaction in the *o*-, *m*- and *p*-positions should be to each other as 2 : 2 : 1. Actually, the ratios are not so simple, because, for example, attack on the *ortho*-position by the reagent is sterically hindered to some extent by the substituent already present.

Estimation of the $P$ value depending on the molecular structure is as yet very difficult in the general case. However the value of $P$ is generally constant for various substitution reactions in the *m*- and *p*-positions [21]. It varies in the case of *o*-substitution, but even here its variations are not great (from 1 to 0.1). Therefore when discussing the factors influencing the rate of substitution in the benzene ring the product $PZ$ may be considered constant or varying at the most within the limits of a single order.

As $e$, $R$ and $T$ are constants, it appears that the influence of the orientants on the rate of substitution in the benzene ring is manifested mainly as a change in the value of the activation energy $E$, consideration of which may be limited to a first approximation.

Such a simplification may be made also because, contrary to the factor $PZ$, the energy of activation $E$ is contained in the numerator of the power index and naturally has a much greater influence on the rate constant $k$, basically determining its magnitude.

The relations for reactions of disubstituted benzene are more complex. Here the rate constant depends equally on the activation energy $E$, and on the pre-exponential factor $PZ$. In the following we will confine ourselves to a consideration of the orientation of monosubstituted benzene only.

Except for a few special cases (page 501), in substitution reactions of monosubstituted benzene the effect of the energy of activation is decisive. A minor change in $E$ is enough to cause a significant change in the rate constant $k$. For example, lowering the activation energy by 2 kcal/mole increases the rate of a chemical reaction at room temperature by thirty times.

Thus, the question of the ratios of *o*-, *m*- and *p*-isomers in substitution reactions in the benzene ring reduces to minor differences in the energies of activation of the three competing reactions of *o*-, *m*- and *p*-substitution.

However, at present the error involved in calculating activation energies is much greater than these differences in $E$, determining the nature of orientation. Because of this the only method of relatively estimating the activation energy of *o*-, *m*-, and *p*-substitution is by a purely qualitative comparison of structures of the corresponding active complexes (see pages 479, 490-492).

Depending on the nature of rupture of covalent bonds in substitution in the benzene ring three types of reaction are possible which may be represented by the following general mechanisms:

Homolytic substitution

(1) $R\cdot + H\overset{\cdot\cdot}{:} C_6H_4X \longrightarrow R{-}C_6H_4X + H\cdot$

Electrophilic substitution

(2) $Y^+ + H\overset{\cdot\cdot}{:} C_6H_4X \longrightarrow Y{-}C_6H_4X + H^+$

Nucleophilic substitution

(3) $Z^- + H\overset{\cdot\cdot}{:} C_6H_4X \longrightarrow Z{-}C_6H_4X + H^-$

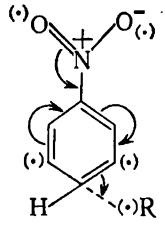
## 8-3.2 Homolytic Substitution in the Benzene Ring

In homolytic substitution the benzene ring is attacked by a neutral radical existing as a kinetically independent particle or arising only in the intermediate stage at the moment of the reaction. Naturally, the point of entry of the radical attacking a molecule of monosubstituted benzene should not depend on the alternating polarity induced by the substituent already present (cf. page 282). However, it is not clear either, at first glance, why radicals substitute for hydrogen atoms predominantly in the *o*- and *p*-positions with respect to the substituent irrespective of whether it is an orientant of the 1st or 2nd kind.

To clear up this question it is necessary to compare the intermediate states arising when a radical attacks the *o*- and *p*-positions, on the one hand, and the *m*-position, on the other.

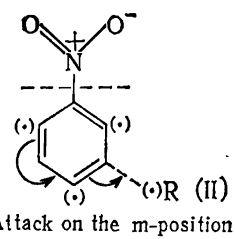
First, let us consider substitution in a molecule containing an orientant of the 2nd kind, say, a nitro group.

An attack on the *p*-position results in intermediate stage (I)* and on the *m*-position, in intermediate stage (II):



(I)

Attack on the p-position



(II)

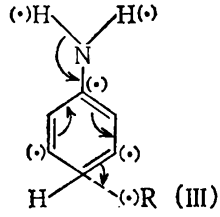
Attack on the m-position

* Arrows here signify shift of a single electron.

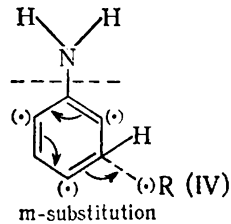
The reaction will proceed predominantly through the transition state with lower energy. The structural features of transition state I which arises when the radical attacks the *para-* (or *ortho-*) position are such, that not only three carbon atoms of the benzene ring, but also two oxygen atoms of the nitro group participate in the delocalization of the unpaired-electron cloud. The transition state II offers fewer possibilities of delocalizing of the unpaired-electron cloud, because in this case the nitro group cannot participate. Consequently, the energy of transition state II is higher than that of transition state I, and radical substitution must occur predominantly in the *para-* (or *ortho-*) position.

Analogous relations arise in reactions of radical substitution when benzene derivatives contain orientants of the 1st kind, e.g., $NH_2$ or $CH_3$.

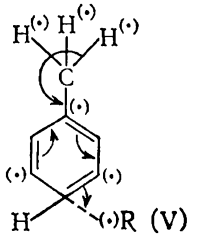
In this case the corresponding transition states may be represented as follows:



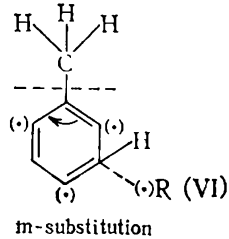

p-substitution




m-substitution




p-substitution

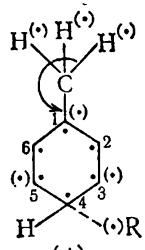



m-substitution

As the substituents $NH_2$ and $CH_3$ do not participate in the delocalization of the unpaired-electron cloud in transition states IV and VI, the energy of these transition states is higher than that of III and V respectively. This is why radical reactions occur predominantly in the *ortho-* (and *para-*) position.

It can be shown in the same way as on page 60 for heterolytic reactions that in the case of homolytic reactions as well, if the benzene ring is represented as a system containing alternating double and single bonds, the same results are obtained as by representing it as a hexagon with six $\pi$ electrons.

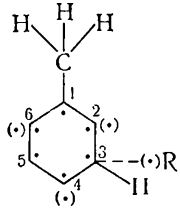
For example, in the radical attack on the *p*-position in the toluene molecule:



(A)

a bond begins to form in the transition state A from the unpaired electron of the radical and the π electron of the 4th carbon atom. Since the π electron of the 4th carbon atom participates in the formation of a bond with the radical its interaction with the π electrons of the 3rd and 5th C atoms weakens, as a result of which the 3rd and the 5th C atoms acquire a certain degree of unsaturation (a nuance of the radical nature). However, as a result of the weakened interaction between the π electrons of the 4th C atom and the π electrons of the 3rd and the 5th C atoms, the interaction between the π electrons of the 3rd and 2nd, and also 5th and 6th C atoms becomes stronger. The latter causes weakening of interaction between the π electrons of the 2nd and 6th C atoms with the π electron of the 1st C atom. This results in the 1st C atom acquiring something of a radical nature. Besides the three carbon atoms of the benzene ring, the hydrogen atoms of the methyl group also take part in delocalizing the unpaired-electron cloud (cf. page 141).

A radical attack on the *m*-position in the toluene molecule results in transition state B:



(B)

in which the possibility of delocalizing the unpaired-electron cloud is smaller (the hydrogens of the methyl group participate no longer).

Hence, this transition state possesses greater energy, and therefore the radical substitution must occur predominantly in the *para*- or *ortho*-position (in the latter case the transition state is quite analogous to A).

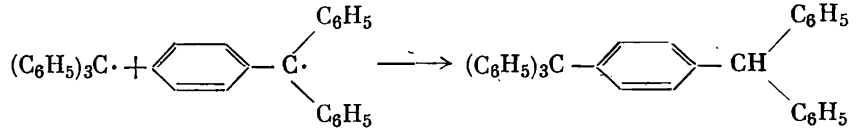
It should be noted that from the radical substitution mechanism concepts discussed, it follows directly that radical substitution of benzene should be more difficult than that of substituted benzenes ($C_6H_5X$), regardless of the nature of the substituent.

Radical substitution must be easier (in the *o*- and *p*-positions) for substituted benzenes, because in the transition state substituents of both the 1st and the 2nd kind participate in delocalization of

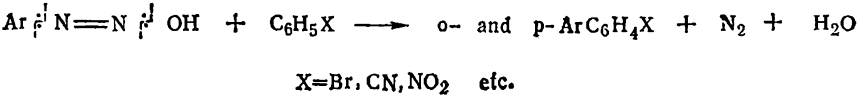
the unpaired-electron cloud. For this reason such reactions must involve a smaller activation energy than radical reactions with unsubstituted benzene.

**Examples of Substitution Reactions Involving a Radical Mechanism.** This type of reactions includes both old reactions, and reactions discovered in recent years.

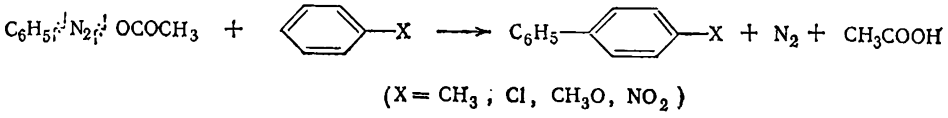
The autocatalytic condensation (under the action of hydrochloric acid) of triarylmethyl free radicals after Chichibabin results in *p*-benzhydryltetraphenylmethane, i.e., radical substitution occurs in the *p*-position [22].



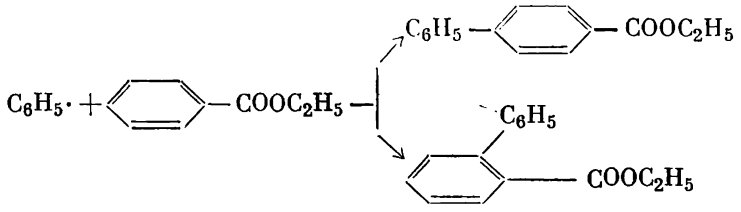
Arylation of benzene derivatives by aryldiazohydrates (Gombeg's reaction) leads to the formation of *o*- and *p*-substituents, regardless of the nature of the orientant [23].



Decomposition of phenyldiazoacetate in a substituted benzene medium always results in *p*-substituted diphenyl derivatives [24]:



Phenyl radicals formed by treating iodobenzene with copper powder in ethyl benzoate solution react with the latter, yielding esters of diphenyl-2 and diphenyl-4-carboxylic acids [25]:



When benzoyl peroxide is decomposed in substituted benzene solution, *o*- and *p*-substituted diphenyls have been found to form.

The following probable mechanism was suggested [25] for reactions of this type:

$$(C_6H_5COO)_2 \longrightarrow 2C_6H_5COO\cdot$$

$$C_6H_5COO\cdot + C_6H_5Cl \longrightarrow C_6H_5COOH + \cdot C_6H_4Cl$$

$$ClC_6H_4\cdot + (C_6H_5COO)_2 \longrightarrow Cl-C_6H_4-C_6H_5 + CO_2 + C_6H_5COO\cdot$$

**Ratios of Isomers Formed in Free Radical Substitution Reactions.** In the above examples only the formation of *o*- and *p*-substitution products was noted.

The theoretical concepts of radical substitution discussed above can account for predominant formation of *o*- and *p*-isomers but not for their exclusive formation.

As the yield of *o*- and *p*-isomers is not quantitative, and *m*-isomers are generally more soluble, it is probable that though they formed, they could not be isolated in the reactions in question.

This assumption was confirmed recently, particularly by spectroscopic analyses of isomer mixtures.

It was shown that radical substitution occurs in the *o*-, *m*-, and *p*-positions, but predominantly in *o*- and *p*-positions.

This was established for the reaction of phenyl radical with nitrobenzene, chlorobenzene, bromobenzene, ethyl benzoate, toluene and other compounds.

It is interesting to note that radical substitution occurs more frequently in the *ortho*- than in the *para*-position.

The amounts of *o*-, *m*-, and *p*-isomers formed by phenylation (with benzoyl peroxide, or phenyldiazonium hydroxide) of various benzene derivatives are shown in Table 8-1. The data were obtained by infrared or ultraviolet spectrophotometry [27].

TABLE 8-1

**Percentage of *o*-, *m*-, and *p*-Isomers Formed in Phenylation of Benzene Derivatives**

| Phenylated Compound | Per cent of Isomers Formed | | |
|---|---|---|---|
| | *ortho* | *meta* | *para* |
| Toluene | 71 | 17 | 12 |
| Fluorobenzene | 53 | 30 | 17 |
| Chlorobenzene | 62 | 24 | 14 |
| Bromobenzene | 50 | 33 | 17 |
| Iodobenzene | 51 | 32 | 17 |
| Diphenyl | 50 | 22 | 28 |
| Nitrobenzene | 58 | 10 | 32 |
| Pyridine | 58 | 27 | 15 |

In accordance with theoretical considerations (pages 479-481) radical substitution in the benzene ring is enhanced by substituents of both the 1st and 2nd kinds.

This is apparent, for instance, from the data of Table 8-2, which gives the partial rate factors* of a number of aromatic compounds

TABLE 8-2

**Partial Rate Factors of Benzene Derivatives in Phenylation Reaction**

| Phenylated Compound | $F_o$ | $F_m$ | $F_p$ |
|---|---|---|---|
| Benzene . . . . . | 1.0 | 1.0 | 1.0 |
| Toluene . . . . . | 4.1 | 1.0 | 1.4 |
| Fluorobenzene . . . | 2.2 | 1.25 | 1.35 |
| Chlorobenzene . . . | 2.7 | 1.03 | 1.2 |
| Bromobenzene . . . | 2.6 | 1.75 | 1.8 |
| Iodobenzene . . . . | 2.8 | 1.7 | 1.8 |
| Nitrobenzene . . . . | 7.0 | 1.2 | 7.9 |
| Pyridine . . . . . | 1.91 | 0.86 | 1.01 |

when the latter are phenylated by benzoyl peroxide or phenyldiazonium hydroxide [27].

The presence of a nitro group especially enhances radical substitution ($F_o = 7.0$; $F_m = 1.2$; $F_p = 7.9$). Thus nitrobenzene and *m*-dinitrobenzene can be methylated by lead tetraacetate to form a mixture of nitrotoluenes and nitroxylenes (page 368). Benzene, chlorobenzene, toluene and naphthalene are not methylated under these conditions but yield normal oxidation products only.

An example of deactivation of radical substitution in $C_6H_5X$ by a substituent X is known [28]. This is phenylation of *tert*-butylbenzene by benzoyl peroxide. In this case $\frac{K_1}{K_0} = 0.87$ ($K_1$ and $K_0$ being the phenylation rates of tertiary

* The partial rate factor ($F$), proposed by Ingold, is a quantitative characteristic of the influence of the substituent X in $C_6H_5X$ upon the rate of substitution compared with the rate of an analogous substitution in benzene. In the general case $F$ is determined as follows. A mixture of $C_6H_5X$ and $C_6H_6$ is subjected to a competing substitution by the action of some reagent, an excess of benzene and substituted benzene being used with respect to the reagent. The relative amounts of substituted benzenes $YC_6H_4X$ and $C_6H_5Y$ are a measure of the relative rates of substitution of $C_6H_5X$ and $C_6H_6$. By comparing these data with the percentage contents of *o*-, *m*- and *p*-disubstituted $YC_6H_4X$ a quantitative expression of the reactivity of the *o*-, *m*-, and *p*-positions ($F_o$, $F_m$ and $F_p$) in $C_6H_5X$ with respect to the positions in unsubstituted benzene is obtained. These are partial rate factors.

butylbenzene and benzene respectively). Deactivation here is due to the large *tert*-butyl group causing steric hindrance to substitution in the *ortho*-positions where radical substitution takes place predominantly (Table 8-1).

Phenylation of *tert*-butylbenzene results in the following amounts of isomeric *tert*-butyl diphenyls:

$$\textit{ortho} = 24\% \quad \textit{meta} = 50\% \quad \textit{para} = 26\%$$
$$F_o = 0.63 \quad F_m = 1.28 \quad F_p = 1.41$$

It should be noted that as the point of substitution of the radical reagent is independent of the electron density in the benzene molecule, the steric hindrance assumes a greater importance in radical substitution than in electrophilic or nucleophilic substitution.

Nitrobenzene is readily hydroxylated by the action of $Fe^{++}$ ion and hydrogen peroxide [29]:

$$C_6H_5NO_2 \xrightarrow{\cdot OH} HO{-}C_6H_4{-}NO_2$$

All three isomers are formed in this reaction but *o*- and *p*-isomers predominate.

Finally, mercuration of substituted benzenes with mercuric acetate [30]

$$Hg(CH_3COO)_2 + C_6H_5X \longrightarrow CH_3COOHgC_6H_4X + CH_3COOH$$

results in the formation of a mixture of isomers in which *o*- and *p*-isomers usually predominate, independently of whether the substituent X is a substituent of the 1st or of the 2nd kind. This reaction is also evidently homolytic (cf. page 518).

Investigation of the phenylation of nitrobenzene (at 125°) and pyridine (at 105°) with different phenylating reagents showed that the isomer ratio generally depends little on the nature of the source of phenyl radicals. Some data are listed in the table below [31].

TABLE 8-3

**Percentage of Isomers Obtained in the Phenylation of Nitrobenzene and Pyridine by Various Reagents**

| Source of radical | Nitrobenzene | | | Pyridine | | |
|---|---|---|---|---|---|---|
| | *ortho* | *meta* | *para* | *ortho* | *meta* | *para* |
| $(C_6H_5COO)_2$ | 56.3 | 15.7 | 28.0 | 54 | 32 | 14 |
| $Pb(C_6H_5COO)_4$ | 55 | 16 | 29.0 | 52 | 32.5 | 15.6 |
| $C_6H_5I(OOCC_6H_5)_2$ | 57.5 | 14 | 28.5 | 58 | 28 | 14 |
| $C_6H_5N(NO)COCH_3$ | | | | 46 | 43 | 11 |
| $C_6H_5N{=}NC(C_6H_5)_3$ | | | | 53 | 31 | 16 |

Such constancy of the isomer ratios is not surprising because phenyl radicals are formed as kinetically independent particles on decomposition of the phenylating substances. Naturally, under the same conditions (solvent, temperature) they react in the same manner.

### Importance of Polar Factors

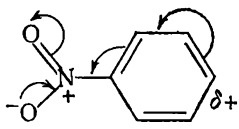
Very interesting results were obtained in a study of the arylating properties of *para*-substituted phenyl radicals. The results of arylation of benzotrichloride at 80° by phenyl, *p*-chlorophenyl and *p*-nitrophenyl radicals [31, 32] are listed in Table 8-4.

TABLE 8-4

**Arylation of Benzotrichloride with X — $C_6H_4$-type Free Radicals**

| Radical | Reference | Per cent of isomers | | |
|---|---|---|---|---|
| | | *ortho* | *meta* | *para* |
| $C_6H_5\cdot$ | [31] | 0 | 60 | 40 |
| $C_6H_5\cdot$ | [32] | 12 | 49 | 39 |
| $p$-$ClC_6H_4\cdot$ | [31] | 0 | 83 | 17 |
| $p$-$O_2NC_6H_4\cdot$ | [31] | 0 | 100 | 0 |
| $p$-$O_2NC_6H_4\cdot$ | [32] | 0 | 73 | 27 |

It is evident that the percentage of *meta*-substitution is higher for the chlorophenyl and particularly the nitrophenyl radical than for unsubstituted phenyl. In other words, the chlorophenyl and nitrophenyl radicals exhibit definite electrophilic properties which is evidence that they are polarized to some extent, for example:




The importance of polar factors in reactions of radical substitution is also quite evident from the results of arylation of nitrobenzene and halobenzenes at 80° [32].

As it is evident from Table 8-5 the ratios of isomeric arylation products changes from the phenyl to the chlorophenyl and nitrophenyl radicals, approaching that of electrophilic substitution reactions.

TABLE 8-5

**Arylation of Nitrobenzene and Halobenzenes**

| Arylated Compound | Radical | Per cent of Isomers | | |
|---|---|---|---|---|
| | | *ortho* | *meta* | *para* |
| $C_6H_5NO_2$ | $C_6H_5\cdot$ | 62.5 | 9.8 | 27.7 |
| $C_6H_5NO_2$ | $p\text{-}ClC_6H_4\cdot$ | 59.0 | 13.8 | 27.2 |
| $C_6H_5NO_2$ | $p\text{-}BrC_6H_4\cdot$ | 57.7 | 13.2 | 29.1 |
| $C_6H_5Cl$ | $C_6H_5\cdot$ | 50.1 | 31.6 | 18.3 |
| $C_6H_5Cl$ | $p\text{-}O_2NC_6H_4\cdot$ | 59.6 | 24.2 | 16.2 |
| $C_6H_5Br$ | $C_6H_5\cdot$ | 49.3 | 33.3 | 17.4 |
| $C_6H_5Br$ | $p\text{-}O_2NC_6H_4\cdot$ | 60.5 | 25.1 | 14.4 |

## 8-3.3 Electrophilic Substitution in the Benzene Ring

Two possible general mechanisms of electrophilic substitution in the aromatic series are considered below. The first of them is that of direct substitution, when substitution into the nucleus of the electrophilic reagent $Z^+$ and elimination of proton take place in a single stage passing through a single transition state (T):

$$Z^+ + Ar{-}H \longrightarrow \underset{(T)}{[Z\cdots\cdots Ar\cdots\cdots H]} \longrightarrow Ar{-}Z + H^+$$

The potential energy of the system changes as shown in Fig. 8-3.

The second possible mechanism of electrophilic substitution is two-stage:

$$\text{(a)}\quad Z^+ + Ar{-}H \longrightarrow \overset{H}{\underset{Z}{\overset{+}{Ar}}} \quad (A)$$

$$\text{(b)}\quad \overset{H}{\underset{(A)\ Z}{\overset{+}{Ar}}} \longrightarrow Ar{-}Z + H^+$$

The first stage (a) consists in the formation of an intermediate product (A) of addition of the electrophilic reagent to the aromatic molecule; in the second stage the complex (A) decomposes eliminating a proton (in the solvated, and not the free state, of course).

In 1950 Melander [56] demonstrated that exchanging hydrogen for tritium in the benzene molecule does not affect the rate of bro-

mination or nitration of benzene (a similar result was obtained when D was substituted for H).

These results are evidence against the mechanism of direct substitution, according to which the C — H bond (C — D or C — T bond, respectively) is broken during the slow stage of the reaction, this supposedly being responsible for the kinetic isotope effect.

The two-stage mechanism must also involve a kinetic isotope effect if the second stage of the reaction (stage *b*) is slow.

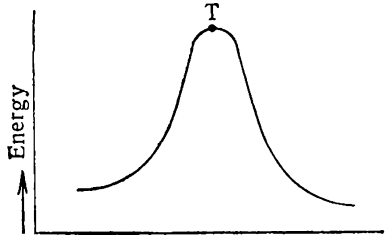



FIGURE 8-3

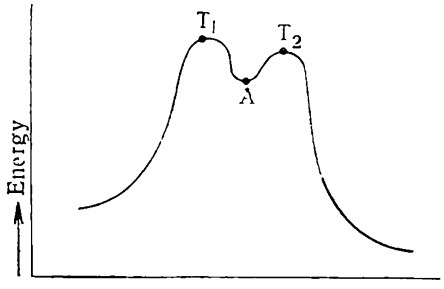


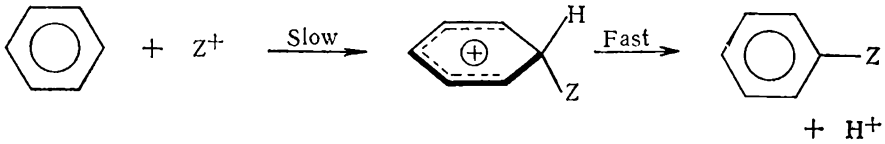

FIGURE 8-4

Thus, the fact that there is no kinetic isotope effect involved in the bromination and nitration of benzene indicates that these are two-stage reactions, the first stage being the slow, rate-determining stage (stage *a*).

The energy change in this case is illustrated by Fig. 8-4.

The maximum $T_1$ on the energy curve corresponds to the first transition state resulting in the formation of the intermediate addition product (A). The second (lower) energetic barrier (transition state $T_2$) is overcome when this addition product is decomposed and the end-product ArZ formed.

In the intermediate addition product (A) one of the carbon atoms of the benzene ring becomes approximately tetrahedral (the C — H and C — Z bonds are located in a plane perpendicular to the plane of the benzene ring). Four π electrons and the positive charge are distributed among the other five carbon atoms.



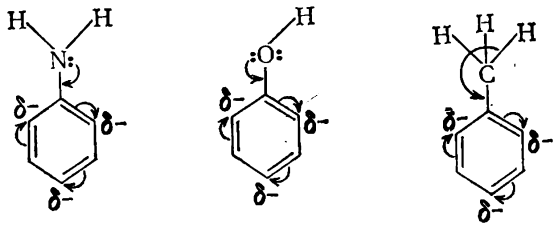

It should be pointed out that the kinetic isotope effect is to be expected when the rates of stages (a) and (b) are similar. This is observed, for instance, in the sulphonation reaction, wherein the

rates of elimination of proton and the $^{+}SO_3H$ group from the intermediate product are comparable (the sulphonation reaction being reversible, as is known):

$$Ar{-}H \leftarrow \overset{+}{Ar}\begin{matrix} \diagup H \\ \diagdown SO_3H \end{matrix} \rightarrow Ar{-}SO_3H$$

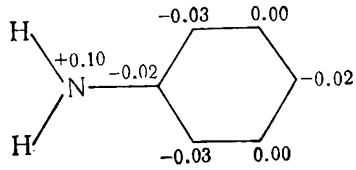
**Distribution of Electron Density in the Molecules of Substituted Benzenes.** Unlike unsubstituted benzene (page 461), in substituted benzenes electron density is unevenly distributed. The symmetry of the electronic cloud of the benzene ring may be disturbed in two substantially opposite ways when a substituent is introduced.

If the substituents are amino, hydroxyl, methyl and other such groups, which according to experimental data are orientants of the 1st kind, the electron density in the benzene ring increases as a whole and particularly in the *o*- and *p*-positions:

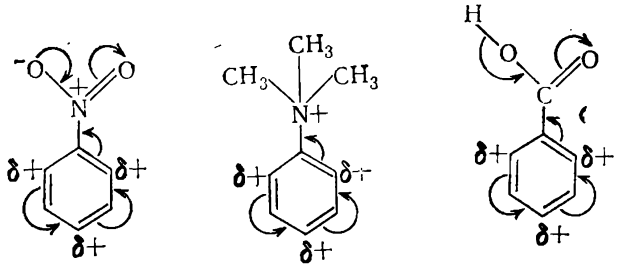


Naturally, the electron shift from the substituents to the benzene ring must affect to a certain extent the nature of both the benzene ring and the substituents. This explains why the hydrogen in the phenol molecule is more mobile than in alcohol molecules where no electron shift from the oxygen to the hydrocarbon radical occurs. Similarly, the free electron pair of the nitrogen in the aniline molecule, being shifted slightly toward the benzene ring, is less effective in binding the proton of an acid; hence the weaker basic properties of aniline compared with fatty amines.

The above mentioned distribution of electron densities in substituted benzenes is confirmed through direct measurement by the magnetic resonance method. The distribution of effective charges may be also calculated by the molecular orbital method. Such a calculation gives the following data for aniline:



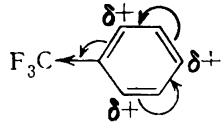
If substituents of the 2nd kind ($NO_2$, $\overset{+}{N}(CH_3)_3$, COOH, etc.) are linked to the benzene ring, the electron density is observed to decrease in the benzene ring as a whole and particularly in the *o*- and *p*-positions:



The presence of partial positive charges on the *o*- and *p*-carbon atoms of the benzene ring tells on the magnitude of the dipole moment. Thus, the dipole moment of nitrobenzene is 3.95 D while that of nitromethane is only 3.40 D.

The above formulas show that positive charges are induced in the *o*- and *p*-positions when an atom carrying a partial or a full positive charge is linked to the benzene ring.

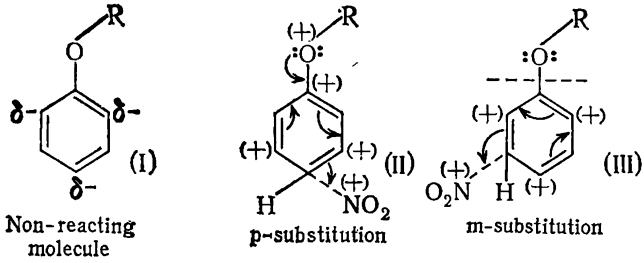
A more complex case is that of benzotrifluoride or benzotrichloride. The strongly negative inductive effect of $CF_3$ and $CCl_3$ does not depend on the presence of an ionic centre, but on the accumulation of strongly electronegative atoms at one atom of carbon which imitates an ionic centre, as it were:



**Distribution of Electron Density at the Moment of Electrophilic Substitution.** Let us first consider electrophilic substitution of substituted benzenes possessing an orientant of the 1st kind. Nitration of phenolic ethers may serve as an example.

The distribution of electron density in the non-reacting molecule of phenolic ether (I) is such that the *o*- and *p*-positions carry partial (effective) negative charges. Therefore the very approach of the electrophilic reagent (for example, nitronium cation) to the *o*- and *p*-carbon atoms is energetically more advantageous than approach to the *m*-carbon atoms. Thus, static factors (distribution of the charges in the non-reacting molecule) favour *ortho*- and *para*-substitution. Besides, attack of the *o*- or *p*-carbon atoms by an electrophilic reagent involves a transition state (II) where the substituent OR participates in the delocalization of the positive charge, along

with the carbon atoms of the benzene ring. But when the *m*-carbon atoms are attacked, because of structural peculiarities, participation of the substituent in the delocalization of the positive charges in the transition state (III) that arises, is impossible.

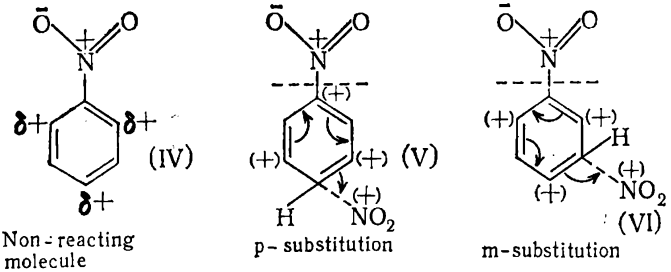



Thus, since the positive charge is less localized in transition state (II) it will be attained at a lower activation energy than transition state (III).

In the example under consideration predominant *o*- and *p*-orientation is the result of the joint action of static (energetically favourable approach of the nitronium cation to the *o*- and *p*-carbon atoms) and dynamic (lower energy of the transition state of *o*- and *p*-substitution) factors.

As substituents of the 1st kind increase the electron density of the benzene ring as a whole (and of the *o*- and *p*-positions in particular), it is to be expected that electrophilic substitution is easier in anilines, phenols, alkylbenzenes, etc., than in unsubstituted benzene.

If a substituted benzene containing an orientant of the 2nd kind (e.g., nitrobenzene) takes part in an electrophilic substitution reaction, approach of the electrophilic reagent to the *m*-positions is energetically more favourable than to the *o*- and *p*-positions.




In the transition states, in both *o*- and *p*-substitutions (V) and in *m*-substitution (VI) delocalization of the positive charge occurs only within the benzene rings without the participation of substituents. As a result, the energies of the transition states (V) and (VI) must

be approximately the same.* Under these conditions the nature of orientation is determined mainly by the static factor, viz., easier approach of the electrophilic reagent to the *m*-carbon atoms.

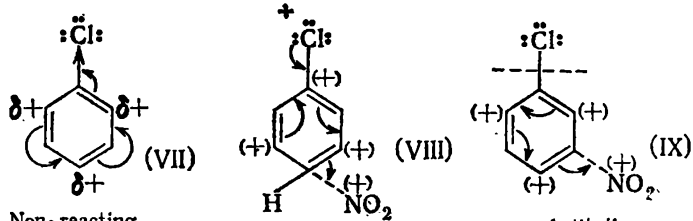
This is the reason for predominant *meta*-orientation.

Since substituents of the 2nd kind impoverish the benzene ring of electrons (*m*-positions included), electrophilic substitution in $C_6H_5X$ (X being an orientant of the 2nd kind) is naturally more difficult than in unsubstituted benzene.

The relations are more complex in the case of electrophilic substitution of halobenzenes, for instance, chlorobenzene.

In the non-reacting molecule of chlorobenzene, like in the vinyl chloride molecule (page 229), the chlorine atom forms the negative end of the dipole. In other words it withdraws electrons from the benzene ring, resulting in partial positive charges (VII) on the *o*- and *p*-carbon atoms. As a result of this, approach of an electrophilic reagent to the *o*- and *p*-carbon atoms is energetically less favourable than approach to the *m*-carbon atoms.

Although the static factors favour *m*-substitution, halogens are *ortho-para*-orientants. This is due to the dynamic factors, which generally play a more important part than static factors.




Non-reacting molecule

p-substitution

m-substitution

Indeed, when an electrophilic reagent attacks the *o*- or *p*-position of chlorobenzene a transition state VIII arises, in which the positive charge is delocalized not only within the benzene ring, but with participation of the chlorine substituent as well. The free valence electrons of the latter are naturally shifted towards the neighbouring carbon atom which carries a partial positive charge. In the transition state IX which arises on *m*-substitution the chlorine atom cannot participate in delocalization of the positive charge. The energy of the transition state VIII is lower than that of IX.

Thus, although the static factors (distribution of charges in the non-reacting molecule) make *o*- and *p*-substitutions more difficult, they take place more readily than *m*-substitution owing to favoura-

* The energy of the transition state of *o*-*p*-substitution must evidently be somewhat larger, because in these cases the partial positive charge arises on the carbon atom linked directly to the like charged nitrogen.

ble dynamic factors: the activation energy of *o*- and *p*-substitution is lower than the activation energy of *m*-substitution.

The unfavourable (for *o*- and *p*-substitution) distribution of charges in the unreacted chlorobenzene molecule manifests itself, however, in the fact that chlorobenzene, like other halobenzenes, is less inclined to electrophilic substitution than benzene itself (which carries no partial positive charges on its carbon atoms).*

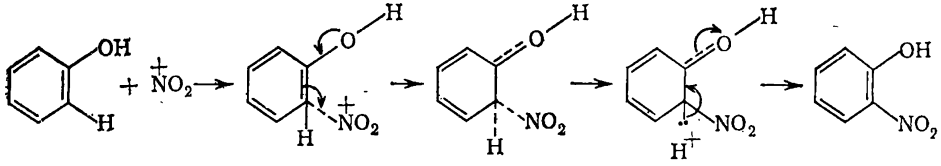
The current theory of orientation just described (for reactions of electrophilic substitution) makes it possible not only to account for the predominant orientation of substituents of the 1st kind in the *o*- and *p*-positions and of substituents of the 2nd kind in the *m*-position, but also (in contrast to the alternating polarity concepts) for the facilitation of electrophilic substitution in the first case, and inhibition in the second. The anomalous behaviour of halides as substituents orienting in the *o*- and *p*-positions, but inhibiting electrophilic substitution is also explained.

It should be noted that extensive experimental data on the direction of orientation in reactions of electrophilic substitution are in satisfactory agreement with the theoretical concepts given above.

When comparing the results of investigations of the substitution mechanism at the unsaturated carbon atom and in the aromatic ring the following circumstance should be pointed out.

As electrophilic substitution reactions at carbon atoms linked with a carbon-carbon double bond take place with retention of configuration (see Chapter 7), it is apparent that no considerable shift of $\pi$ electrons takes place in the transition state (the double bond is not destroyed), because this would have caused a change in configuration. In substitutions of this type an important part is played, evidently, by the $\sigma$-electron pair binding the substituted atom with the unsaturated carbon atom.

It is not very likely that the mechanism of electrophilic substitution at an olefinic carbon atom is fundamentally different from the mechanism of electrophilic substitution in the aromatic series. In the generally accepted concepts of the mechanism of electrophilic substitution in the aromatic series described above the role of the $\sigma$-electron pair binding the substituted atom to the aromatic nucleus is not taken into consideration, e.g.:



It may be supposed [33] that the role of the $\sigma$-electron pair binding the substituent atom with the aromatic ring is more important than is thought at present.

* The reasons for the peculiarities of electrophilic substitution of halobenzenes are quite analogous to the reasons considered above for the addition of hydrogen halides to vinyl halides according to Markovnikov's rule (page 229).

TABLE 8-6

**Percentages of *o*-, *m*- and *p*-Isomers Formed in Nitration, Sulphonation and Halogenation Reactions**

| Reacting Aromatic Compound | Entering Substituent | Resulting Compound | (% *o*-, % *p*-, % *m*-isomers) |
|---|---|---|---|
| Toluene | Nitro group | $NO_2C_6H_4CH_3$ | (56.0; 40.9; 3.1) |
| Ditto | Bromine | $BrC_6H_4CH_3$ | (39.7; 60.3; 0.0) |
| Ditto | Sulpho group | $HO_3SC_6H_4CH_3$ | (31.9; 62.0; 6.1) |
| Chlorobenzene | Chlorine | $C_6H_4Cl_2$ | (39.0; 55.0; 6.0) |
| Ditto | Nitro group | $NO_2C_6H_4Cl$ | (30.1; 69.9; 0.0) |
| Ditto | Bromine | $BrC_6H_4Cl$ | (11.2; 87.2; 1.6) |
| Ditto | Sulpho group | $HO_3SC_6H_4Cl$ | (0.0; 100.0; 0.0) |
| Bromobenzene | Chlorine | $ClC_6H_4Br$ | (45.1; 52.5; 2.4) |
| Ditto | Nitro group | $NO_2C_6H_4Br$ | (37.6; 62.4; 0.0) |
| Ditto | Bromine | $C_6H_4Br_2$ | (13.1; 85.1; 1.8) |
| Ditto | Sulpho group | $HO_3SC_6H_4Br$ | (0.0; 100.0; 0.0) |
| Phenol | Chlorine | $ClC_6H_4OH$ | (49.8; 50.2; 0.0) |
| Ditto | Nitro group | $NO_2C_6H_4OH$ | (40.0; 60.0; 0.0) |
| Ditto | Bromine | $BrC_6H_4OH$ | (9.8; 90.2; 0.0) |
| Phenyl fluoride | Nitro group | $NO_2C_6H_4F$ | (12.0; 87.0; 1.0) |
| Phenyl iodide | Ditto | $NO_2C_6H_4I$ | (41.0; 59.0; 0.0) |
| Benzyl fluoride | Ditto | $NO_2C_6H_4CH_2F$ | (28.0; 54.0; 18.0) |
| Benzyl chloride | Nitro group | $NO_2C_6H_4CH_2Cl$ | (32.0; 54.0; 14.0) |
| Benzyl cyanide | Ditto | $NO_2C_6H_4CH_2CN$ | (17.0; 69.0; 14.0) |
| Ethyl phenylacetate | Ditto | $NO_2C_6H_4CH_2COOC_2H_5$ | (32.0; 58.0; 10.0) |
| α,α-Dichlorotoluene | Ditto | $NO_2C_6H_4CHCl_2$ | (23.0; 43.0; 34.0) |
| Benzotrichloride | Ditto | $NO_2C_6H_4CCl_3$ | (6.8; 29.0; 64.0) |
| Benzaldehyde | Ditto | $NO_2C_6H_4CHO$ | (~19.0; ~9.0; 72.0) |
| Acetophenone | Ditto | $NO_2C_6H_4COCH_3$ | (30.0; —; 68.0) |
| Benzoic acid | Ditto | $NO_2C_6H_4COOH$ | (18.5; 1.3; 80.2) |
| Ethylbenzoate | Ditto | $NO_2C_6H_4COOC_2H_5$ | (28.3; 3.3; 68.4) |
| Benzamide | Ditto | $NO_2C_6H_4CONH_2$ | (27.0; ~3.0; 70.0) |
| Benzoyl chloride | Ditto | $NO_2C_6H_4COCl$ | (8.0; ~2.0; 90.0) |
| Benzonitrile | Ditto | $NO_2C_6H_4CN$ | (17.0; ~2.0; 81.0) |
| Nitrobenzene | Ditto | $C_6H_4(NO_2)_2$ | (6.4; 0.3; 93.3) |

It is very important to determine as exactly as possible the relative amounts of isomers formed in various reactions of electrophilic substitution. Such data could give a better idea of the relative orienting power of different substituents.

Table 8-6 shows the quantities of *o*-, *m*-, and *p*-isomers formed in some nitration, sulphonation and halogenation reactions.

It should be noted that no conclusion can be made from the data given in the table regarding the influence of the substituents on the *o*-, *m*-, and *p*-positions of the benzene ring.

The fact that, say, in the nitration of toluene 56.0% of *ortho*-, 40.9% of *para*-, and only 3.1% of *meta*-isomers are formed may be accounted for in two ways: either the methyl group activates the *ortho*- and *para*-positions (relative to benzene), or it passivates the *m*-positions.

Quantitative investigations of the influence of some groups on the reactivity of various positions of aromatic nuclei were carried out by Ingold and coworkers [34]. The relative rate of nitration was studied by nitrating mixtures of benzene and some of its $C_6H_5X$ derivatives with an insufficient (for complete nitration of both substances) quantity of nitric acid. The relative quantities of $XC_6H_4NO_2$ and $C_6H_5NO_2$ were then determined, and this was a measure of the relative rates of nitration of $C_6H_5X$ and benzenes (the relative rates are given in Table 8-7).

TABLE 8-7

**Relative Rates of Nitration of Benzene Derivatives**

| Aromatic Compound | Rate | Aromatic Compound | Rate |
|---|---|---|---|
| Benzene | 1.00 | Chlorobenzene | 0.033 |
| Toluene | 24.5 | Bromobenzene | 0.030 |
| *tert*-Butylbenzene | 15.7 | Iodobenzene | 0.18 |
| Ethyl phenylacetate | 3.66 | Cinnamic acid | 0.111 |
| Ethyl benzoate | 0.00367 | Benzyl chloride | 0.302 |
| Fluorobenzene | 0.15 | | |

The rates of nitration given in Table 8-7 are the sums of the rates of substitution into all the positions.

By multiplying these rates* by numbers expressing the proportions in which the *o*-, *m*- and *p*-isomers are formed, numerical values are obtained (the partial rate factors—$F_o$, $F_m$ and $F_p$) characterizing the relative rates of nitration of the separate positions of the aromatic rings (the rate of nitration of each separate position of the benzene ring equals one).

* In this case, for convenience, the rates given in Table 8-7 have been multiplied by 6.

TABLE 8-8

**Relative Substitution Rates at Different Positions of the Aromatic Ring (Partial Rate Factors) in the Nitration of Benzene Derivatives**

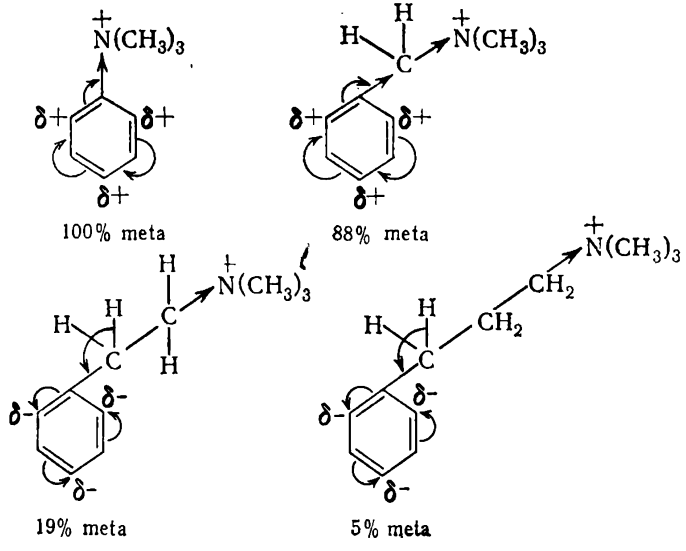
| Nitrated Compound | $F_o$ | $F_m$ | $F_p$ |
|---|---|---|---|
| Benzene . . . . . | 1.0 | 1.0 | 1.0 |
| Toluene . . . . . | 42.0 | 2.5 | 58 |
| Ethyl phenylacetate | 4.62 | 1.16 | 10.4 |
| Benzyl chloride . . . | 0.200 | 0.140 | 0.951 |
| Chlorobenzene . . . . | 0.030 | 0.00 | 0.139 |
| Bromobenzene . . . . | 0.037 | 0.00 | 0.106 |
| Ethyl benzoate . . . | 0.0026 | 0.0079 | 0.0009 |

The experimental data given in Table 8-8 reveal that $CH_3$ and $CH_2CO_2C_2H_5$ activate the benzene ring as a whole and the *p*-position in particular. The substituents Cl, Br and $CH_2Cl$ passivate the benzene ring as a whole, but most of all, the *m*-position.

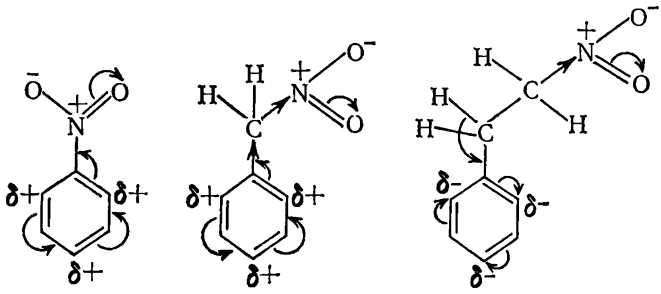
Contrariwise, the substituent $CO_2C_2H_5$ passivates the *o*- and *p*-positions more than the *m*-position.

It is interesting to note the gradual weakening of the influence of the orientant as the number of saturated carbon atoms between the orientant and the benzene ring grows.

Thus, nitration of four aromatic ammonium cations showed the following percentages of *m*-derivatives to form:

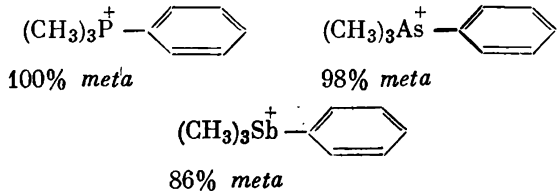


In the two last cases the trimethylaminoethyl and trimethylaminopropyl groups orient as if they were alkyl groups because the inductive effect of the trimethyl ammonium group diminishes rapidly along the chain of saturated carbon atoms. Similar results* are obtained when nitro compounds of like structure are nitrated:



93% meta 67% meta 13% meta

Comparison of the yields of *meta*-derivatives in nitrating quaternary salts of phosphonium, arsonium and stibonium shows that the influence of the positive charge on the benzene ring weakens with increasing atomic radius and number of electronic shells screening the ionic charge:

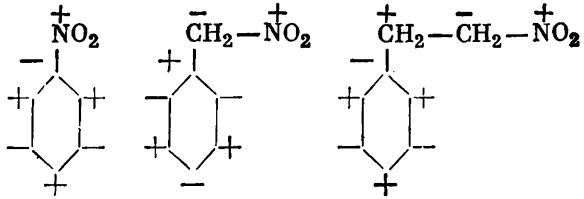


100% *meta* 98% *meta*

86% *meta*

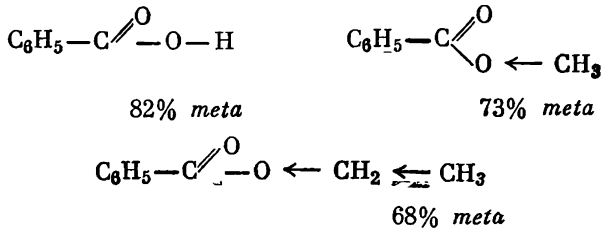
Even small differences in the electronic nature of the substituents are reflected in the yields of the isomeric products of electrophilic

* It should be noted that such results cannot be explained on the basis of the alternating polarity concept.

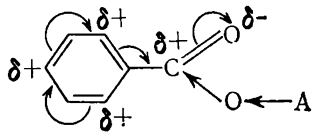


According to these concepts the percentage of the *m*-derivative in the case of nitrotoluene where the *m*-carbon atoms are positively charged, should be lower than the percentage of the nitro derivative in the case of β-nitroethylbenzene where the *m*-carbon atoms are negatively charged.

substitution. For example, nitration of benzoic acid and its methyl and ethyl esters results in the following percentages of *meta*-derivatives:




The difference in influence of the hydrogen, methyl and ethyl on the reactivity of the benzene ring (with which they are not directly linked) is explained below. In compounds of this type:



the orienting influence of the substituent depends on the magnitude of the positive charge on the carbon of the carboxyl group: the larger it is, the more positive are the charges of the *o*- and *p*-carbon atoms of the benzene ring and consequently the more favourable are the conditions for *m*-substitution. Decrease of this positive charge as a result of increase of the positive inductive effects of groups A must result in lowering of the percentage of *m*-derivatives. It is known that electron-repelling properties increase in the sequence $H < CH_3 < C_2H_5$. This is the reason why the percentage of *meta*-substituents drops.

**Correlation of *ortho-para*-Isomers in Reaction Products During Electrophilic Substitution.** It is known that in reactions of electrophilic substitution of benzene derivatives containing orientants of the 1st kind, *ortho-para*-isomers are formed predominantly. It is interesting and important to know what factors influence the ratio of *ortho*- and *para*-isomers.

As there are two *ortho*-positions and only one *para*-position, if the substituent exerted an equal influence on all these positions one would expect twice as much of the *ortho*-isomer to form as the *para*-isomer. However, actually the *o*/*p*-isomer ratio is not only less than 2, but most often *p*-isomers predominate.

Table 8-9 shows the *ortho-para* ratios for various reactions of electrophilic substitution.

TABLE 8-9

**Relative Amounts of *o*- and *p*-Isomers Obtained in Reactions of Electrophilic Substitution**

| Compound | Reaction | *ortho-para* Ratio |
|---|---|---|
| Toluene | Nitration | 1.4 |
| | Bromination | 0.7 |
| | Sulphonation | 0.5 |
| Chlorobenzene | Nitration | 0.4 |
| | Chlorination | 0.7 |
| | Bromination | 0.1 |
| | Sulphonation | 0.0 |
| Bromobenzene | Nitration | 0.6 |
| | Chlorination | 0.9 |
| | Bromination | 0.2 |
| | Sulphonation | 0.0 |
| Phenol | Nitration | 0.7 |
| | Chlorination | 1.0 |
| | Bromination | 0.1 |
| Acetanilide | Nitration | 0.1 |
| Benzanilide | Nitration | 0.0 |
| Benzyl chloride | Nitration | 0.7 |

It is logical to assume, first of all, that as the size of the substituent X in benzene derivatives $C_6H_5X$ increases *ortho*-substitution will become more and more difficult, and *para*-substitution, more

TABLE 8-10

**Effect of Steric Hindrance on the Ratios of *ortho-para*-Isomers (in Nitration of Benzene Homologues)**

| Alkyl Benzene | *o*-isomer : *p*-isomer ratio (according to data of various authors) | | | |
|---|---|---|---|---|
| | [35, 36] | [37, 38] | [39] | [40] |
| Toluene . . . . . | 1.57 | 1.5 | 1.42 | 1.4 |
| Ethylbenzene . . . . . | 0.93 | 1.2 | — | 1.1 |
| Isopropylbenzene . . . . | 0.48 | 1.16 | — | 0.35 |
| *tert*-Butylbenzene . . . . | 0.22 | — | 0.15 | — |

and more easy. This is observed in the nitration of alkyl benzenes with alkyl groups increasing in size from methyl to tertiary butyl (see Table 8-10).

The second factor which should affect the *ortho-para*-isomer ratio, is the size of the entering substituent: as it increases *o*-substitution should be inhibited and consequently the *ortho-para*-isomer ratio should decrease.

This may account for the fact that in chlorination of chlorobenzene, bromobenzene and phenol the *ortho-para*-isomer ratios are 0.7, 0.9 and 1.0 respectively while in bromination of the same substances these ratios are much smaller, namely 0.1; 0.2; 0.1.

Besides steric factors, *ortho-para*-isomer ratios are doubtlessly affected by electronic factors. Thus, when phenyl halides are nitrated, the ratio grows from phenyl fluoride to phenyl iodide, though the size of the halogen substituent increases in the same sequence (see Table 8-11).

TABLE 8-11

**Dependence of *ortho-para*-Isomer Ratios on Electronegativity of Halides (in Nitration)**

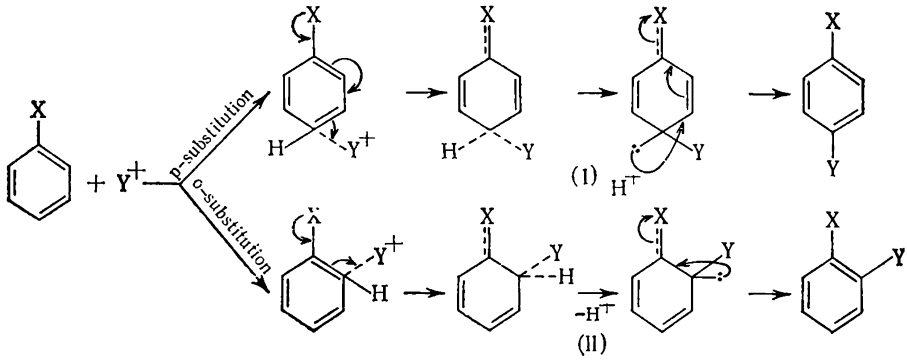
| Phenyl Halide | % *ortho* | % *para* | *o/p* |
|---|---|---|---|
| Phenyl fluoride | 12 | 87 | 0.14 |
| Phenyl chloride | 30 | 70 | 0.43 |
| Phenyl bromide | 38 | 62 | 0.60 |
| Phenyl iodide | 41 | 59 | 0.69 |

Such a change in *ortho-para*-isomer ratios can be understood if it is taken into consideration that the electronegativity of halides decreases in the sequence $F > Cl > Br > I$. The more electronegative the halogen is the more the *ortho*-positions will be deactivated. The carbon atom in the *para*-position is farther removed from the halogen and it is, therefore, less deactivated.

In conclusion it should be pointed out that in the general case a substantial factor determining the predominant formation of *p*-isomers in various electrophilic substitution reactions is that *p*-substitution should require a smaller energy of activation than *o*-substitution.

The *p*-substitution of a substance of the type $C_6H_5X$ takes place through the transition state I, and *o*-substitution, through the

transition state II:




It is apparent that transition state I is similar to *p*-benzoquinone and transition state II is similar to *o*-benzoquinone.

As *p*-quinones are more stable (possessing, for instance, a lower reduction potential) than *o*-quinones, it is clear that transition state I will form easier than II. As a result of this, *p*-substitution should occur faster than *o*-substitution.

In spite of the fact that many aspects of the problem of *ortho-para*-isomer ratios become clear from the above discussion, it is, on the whole, a complicated question which cannot at present be considered fully explained.

**Effect of Reaction Conditions in Electrophilic Substitution.** The effect of reaction conditions on orientation in electrophilic substitution in the benzene ring was thought to be of secondary importance for a long time. It was accepted, for instance, that a variation in the temperature of halogenation or nitration could not change the type of orientation (*ortho-para*, or *meta*-), and could effect only minor changes in *o*-, *p*-, *m*-isomer ratios.

It was found, however [41], that a strong rise in the bromination temperature of bromobenzene (above 450°) changes the type of orientation, yielding predominantly *m*-dibromobenzene. Variations in the percentage yields of isomers are given in Table 8-12.

This phenomenon is due to the fact that at high temperatures, besides the energy of activation, the pre-exponential factor of the basic kinetic equation begins to play an important part.

On page 478 it was shown that the rate constants of two reactions differing by 2 kcal/mole in their activation energies at room temperature are in a ratio of thirty to one. However at 500° the rate constant ratio is no longer 30 : 1 but 3.65 : 1, or 8 times smaller. In this case the influence of the pre-exponential factor can no longer be ignored. If we take into consideration that there is only one *p*-position, and that the *o*-positions are sterically hindered, the

TABLE 8-12

**Yields of Isomeric Dibromobenzenes at Various Temperatures**

| Isomers \ Temperature | 400° | 450° | 500° | 585° | 630° |
|---|---|---|---|---|---|
| *Ortho* . . . . . | 20 | 20.5 | 20.9 | 19.6 | 18.9 |
| *Meta* . . . . . | 23 | 54.5 | 55.7 | 58.8 | 59.9 |
| *Para* . . . . . | 57 | 25 | 23.4 | 21.6 | 21.2 |

*m*-bromination of bromobenzene at high temperature can be accounted for.*

For the same reasons pyridine behaves like bromobenzene at high temperatures. Bromination of pyridine at 500° results in α-bromopyridine [42] and nitration at a high temperature results in α-nitropyridine [43].

The effect of solvents and catalysts on electrophilic substitution in the aromatic series has been studied comparatively little. In the

TABLE 8-13

**Influence of Catalysts on Isomer Ratios in the Halogenation of Benzene Derivatives**

| Reacting Compound | Reaction | Catalyst | Per cent of Isomers Formed | | |
|---|---|---|---|---|---|
| | | | *ortho* | *meta* | *para* |
| Phenyl chloride | Chlorination | $AlCl_3$ | 30 | 4 | 66 |
| Ditto | Ditto | $FeCl_3$ | 39 | 5 | 56 |
| Ditto | Bromination | None | 18 | 1 | 81 |
| Ditto | Ditto | $AlBr_3$ | 15 | 9 | 76 |
| Ditto | Ditto | $FeBr_3$ | 11 | 2 | 87 |
| Phenyl bromide | Chlorination | $AlCl_3$ | 30 | 5 | 65 |
| Ditto | Ditto | $FeCl_3$ | 42 | 7 | 51 |
| Ditto | Bromination | $AlCl_3$ | 8 | 30 | 62 |
| Ditto | Ditto | $FeCl_3$ | 13 | 2 | 85 |
| oluene | Ditto | None | 39.7 | 0 | 60.3 |
| Ditto | Ditto | $AlCl_3$ | 40.0 | 0 | 60.0 |

* At such high temperatures the reaction mechanism becomes radical rather than electrophilic.

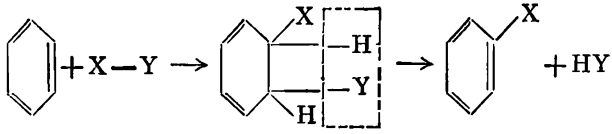
great majority of cases they are apparently unable to change the qualitative picture of orientation, and change the ratio of the reaction products within narrow limits (Table 8-13).

However a few examples are known where the nature of orientation is changed by catalysts. One of them is the sulphonation of anthraquinone after Ilyinsky [44], wherein α-anthraquinone sulphonic acid forms in the presence of a mercury catalyst instead of the β-sulpho acid. Another example is sulphonation of benzenesulphonic acid, when the presence of mercury boosts the yield of the *p*-isomer by more than 15 times [45]. Possibly, such a considerable effect of the catalyst in the two cases mentioned is due to the ionic mechanism of sulphonation changing to a radical one.

## 8-3.4 Individual Reactions of Electrophilic Substitution

Among reactions of electrophilic substitution are reactions of nitration, halogenation, sulphonation, mercuration, acylation, diazonium coupling, chloromethylation, and deuteroexchange. The mechanisms of the most important of them are considered below.

In the twenties Wieland developed concepts according to which substitution in the benzene ring (nitration, sulphonation, halogenation) is preceded by addition (see [46]):



The analogy with the addition of nitric acid to ethylene and α, α′-diphenylethylene was given as a proof of this reaction mechanism:

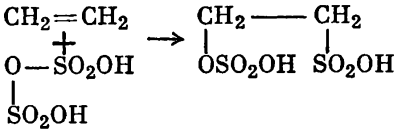
$$(C_6H_5)_2C{=}CH_2 \xrightarrow[\text{Glacial } CH_3COOH]{HNO_3} (C_6H_5)_2C(OH)-CH_2(NO_2) \longrightarrow (C_6H_5)_2C{=}CH-NO_2 + H_2O$$

It was shown later, however, that in the absence of nitrogen oxides nitric acid adds neither to ethylene nor to its homologues, and that it can only oxidize or polymerize them. At −20° pure nitric acid adds to isobutylene but as $H-ONO_2$ and not $HO-NO_2$. In the presence of sulphuric acid it adds as $NO_2-OSO_3H$ rather than $HO-NO_2$.

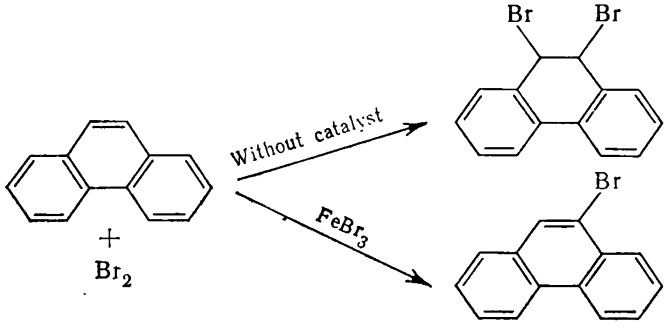
Further Wieland considered that ethylene reacts with sulphuric acid as follows:

$$CH_2{=}CH_2 + HO-SO_2OH \longrightarrow CH_2(OH)-CH_2(SO_2OH) \xrightarrow{HOSO_2OH} CH_2(OSO_2OH)-CH_2(SO_2OH) + H_2O$$

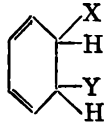
Actually it was found that ethylene adds only pyrosulphuric acid and not sulphuric acid:



As an argument in favour of preliminary addition of halogen in the halogenation of aromatic compounds phenanthrene was often mentioned. It readily yields 9,10-dibromophenanthrene which is easily transformed into 9-bromophenanthrene with elimination of hydrogen bromide. However, Price [47] showed that the formation of dibromide and 9-bromophenanthrene are two unrelated reactions:

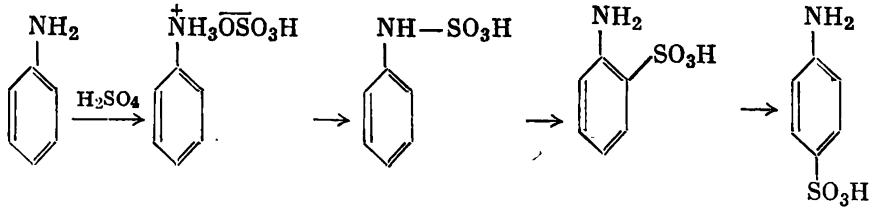



Thus there are no experimental data in support of preliminary addition of the reagent to the aromatic ring in the course of substitution reactions. From the theoretical point of view such an addition is particularly improbable in the case of the benzene ring because it would destroy the stable "benzenoid" electronic configuration and give rise to relatively localized $\pi$ electrons in the compound




Another widely accepted point of view is that in the presence of an active group (OH, $NH_2$, etc.) the substituents do not attack the benzene ring directly, but react first with the orienting group. The compounds thus formed are transformed directly into the final substitution products.

Sulphonation of aniline may serve as an example in favour of this point of view. It actually proceeds as follows:



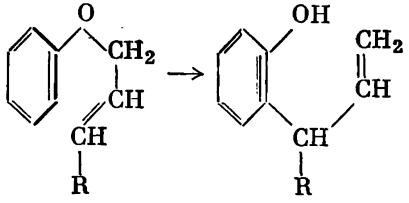
A similar rearrangement consisting of transfer of a group of atoms from the side chain into the benzene ring may occur in other intermediate compounds as well:

$$RNH \cdot NO_2,\ RO - SO_3H,\ RNH - OH,\ RNH - CH_3,\ \text{etc.}$$

Although the fact that in the sulphonation of aniline the sulpho group migrates from the side chain into the nucleus arouses no doubts, the hypothesis mentioned is untrue in general.

It is easy to show, for instance, that alkylation of phenols is a direct ring substitution reaction.

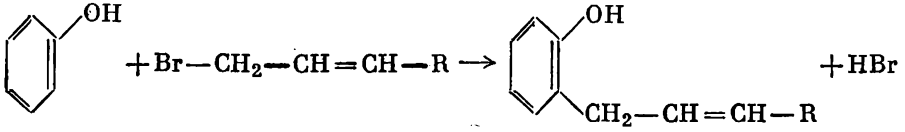
Thus if allylphenyl ether is subjected to a Claisen rearrangement:



(A)

an *o*-allylphenol derivative (A) results.

But direct alkylation of phenol gives an allylphenol (B) of a different structure:



(B)

It is thus apparent that alkylation of phenols involves direct substitution into the ring.

Convincing facts of direct reaction of the reagent with the ring, rather than with the orientant may be found in diazonium coupling.

For example, tertiary amines $C_6H_5NR_2$ couple with diazonium salts just as readily as primary and secondary. In this case intermediate formation of the reaction product of the diazonium compound with the orientant is impossible. Phenolic ethers and even certain hydrocarbons enter into diazo coupling reactions, where no intermediate products can be formed either.

From the discussion above it follows that the substitution reaction in the benzene ring does not take place through an intermediate addition product or by migration of the substituent, but directly into the ring.

**Nitration.** The mechanism of nitration has been studied in detail only recently.

Nitration is generally accomplished by the action of a nitrating mixture consisting of concentrated nitric and sulphuric acids, on the aromatic compound:

$$Ar-H + HNO_3 \xrightarrow{H_2SO_4} Ar-NO_2 + H_2O$$

A number of investigators held that the function of the sulphuric acid was to bind the water formed. It was shown, however, that the rate of nitration depends chiefly on the acidity of the medium and not on its water-binding properties. Thus the reaction rate is maximal when 90% and not 100% sulphuric acid is used. The addition of phosphorus pentoxide, a strong dehydrating agent, has no effect on the reaction rate.

Finally, the dehydrating properties of the medium influence the rate when water is formed in a reversible reaction. But nitration is an irreversible reaction.

As early as 1903 Euler [48] suggested that the actual nitrating agent is not nitric acid but nitronium ion. But this idea was not confirmed experimentally until recently.

Measurements of the melting point lowering of solutions of nitric acid in sulphuric acid showed the van't Hoff factor $i$ to be equal to 4. This means that on reacting with the solvent, sulphuric acid, each molecule of nitric acid yields four dissolved particles.

The only possible explanation of this is that nitric acid reacts with sulphuric acid according to the equation [49]:

$$HNO_3 + 2H_2SO_4 \rightleftarrows NO_2^+ + H_3O^+ + 2HSO_4^-$$

Similarly, the van't Hoff factor for solutions of nitrogen pentoxide in sulphuric acid is 6 which indicates that ions form according to the following equation:

$$N_2O_5 + 3H_2SO_4 \longrightarrow 2NO_2^+ + H_3O^+ + 3HSO_4^-$$

The dissociation is also confirmed by the high electrical conductivity of solutions of nitric acid or nitrogen pentoxide in sulphuric acid and by a study of their Raman spectra.

Proof of the existence of nitronium ion is by no means proof that the nitrating agent is specifically $NO_2^+$ and not undissociated nitric acid.

However, the results of a number of kinetic investigations of the nitration reaction suggest the conclusion that it is specifically the nitronium ion which is the nitrating agent.

In the general case, the rate of nitration in sulphuric acid is proportional to the concentrations of nitric acid and the aromatic compound:

$$v = k_2[ArH][HNO_3]$$

However, in organic solvents (in the absence of sulphuric acid) nitration of sufficiently reactive aromatic compounds proceeds like a zero-order reaction (though the reaction rate depends on the

quantity of nitric acid taken for the reaction, it remains constant in the course of the process):

$$v = k_0[HNO_3] = \text{const}$$

Thus, the aromatic compound does not participate in the rate-determining step. This indicates that the measured rate is the rate of transformation of nitric acid into the reagent which then rapidly attacks the aromatic compound. This electrophilic reagent can be nothing but nitronium ion.

When less reactive compounds such as chlorobenzene are nitrated under these conditions, the order of the reaction becomes different from zero, and in the case of very unreactive compounds (ethyl benzoate, *p*-dichlorobenzene) nitration proceeds as a first-order reaction:

$$v = k_1[ArH][NHO_3] = \text{const}$$

Addition of strong acids accelerates the reaction; when a large quantity of sulphuric acid is added, nitration becomes a second-order reaction. Addition of nitrate ion inhibits the reaction.

It is natural to assume that the acceleration and deceleration of nitration on addition of strong acids and nitrate ion is due to an increase or the decrease of the nitrating reagent in the mixture.

In a neutral organic solvent autoionization occurs according to the equations below:

$$2HNO_3 \overset{\text{Fast}}{\rightleftharpoons} H_2NO_3^+ + NO_3^-$$

$$H_2NO_3^+ \overset{\text{Slow}}{\rightleftharpoons} NO_2^+ + H_2O$$

Addition of a strong acid should increase the number of nitronium ions and lower the number of nitrate ions because of the reaction:

$$NO_3^- + H_2SO_4 \rightleftarrows HNO_3 + HSO_4^-$$

$$HNO_3 + 2H_2SO_4 \rightleftarrows NO_2^+ + H_3O^+ + 2HSO_4^-$$

Conversely, the addition of nitrate ions would suppress dissociation and thus lower the number of nitronium ions.

Hence the reaction rate depends specifically on the quantity of nitronium ions.

The process of nitration consists in a proton being forced out by a nitronium ion and combining with a base B [50]:

$$ArH + \overset{+}{N}O_2 + B \longrightarrow ArNO_2 + HB^+$$

The base may be nitrate ion, bisulphate ion or a water molecule.

The change in the order of the reaction is due to the change in the ratio of the rate of autoionization of the acid to the rate of reaction of nitronium ion with the aromatic compound.

In the case of a reactive aromatic compound which binds the nitronium ions as they form, the velocity of the process is determined by the rate of autoionization and by the total number of nitronium ions in equilibrium with the free acid. If nitric acid is present in great excess, the part that is used up in the reaction has no perceptible effect on the nitronium-ion concentration and therefore the rate of the process depends only on the initial concentration of acid and remains constant during the process, that is, the reaction is a *zero-order* one.

In the case of an unreactive compound the velocity of the process is determined by the rate of reaction of this compound with nitronium ion. Since the nitronium-ion concentration remains practically constant when an excess of acid is used, the rate of the process is determined by the concentration of the nitrated compound, which changes in time, i.e., here we have to do with a *first-order* reaction.

Under ordinary conditions in the presence of a large amount of a strong acid, causing complete ionization of the nitric acid, and a small excess of the latter, the reaction becomes *second-order*.

The above discussion leaves unclear why nitration proceeds faster in solutions containing a certain amount of water, i.e., in solutions having a definite acidity.

The explanation of this phenomenon is as follows: in sulphuric acid the bases binding the proton freed during nitration may be bisulphate ion, sulphuric acid, and in oleum—also pyrosulphate ion $HS_2O_7^-$. Their basic properties decrease in the sequence:

$$HSO_4^- > H_2SO_4 > HS_2O_7^-$$

Thus, the highest reaction rate should be expected at maximum concentration of bisulphate ion, that is, in 80% sulphuric acid. However, under such conditions the amount of nitronium ions formed is small, and therefore the optimum acid concentration is that which gives the lowest acidity of the mixture at which nitric acid is completely transformed into nitronium ion.

The optimum conditions of nitration depend to a certain extent on the nature of the substance being nitrated. Thus, phenol can be nitrated in dilute acid; the fastest rate of nitration of nitrobenzene is attained in 90% sulphuric acid, and of β-naphthalenesulphonic acid, in 95% sulphuric acid.

The dependence of the optimum acidity on the nature of the substance being nitrated is due to the fact that in strongly acid solution the organic compound ionizes, forming cations which repel the nitronium ions and slow down the nitration reaction.

Thus optimum conditions are determined by competition between two equilibrium processes:

$$HNO_3 + 2H_2SO_4 \rightleftarrows \overset{+}{N}O_2 + H_3O^+ + 2HSO_4^-$$

$$ArH + H_2SO_4 \rightleftarrows ArH_2^+ + HSO_4^-$$

It follows that the more difficult it is for a substance to add a proton, the more acid a solution is needed to attain the maximum rate of nitration.

Phenol adds a proton relatively easily, forming an oxonium cation $C_6H_5\overset{+}{O}H_2$. This process proceeds to a noticeable extent even in 50% sulphuric acid. However in such a solution nitric acid dissociates predominantly into nitrate ions. Nitronium ions begin to form perceptibly in 60% sulphuric acid.

Therefore, in the case of phenol competition between the equilibrium processes should start approximately in that region of acidity. Indeed, phenol is nitrated fastest in 60-70 % sulphuric acid.* α- and β-Naphthalenesulphonic acids are stronger acids than nitric. It is natural to expect that in these cases organic cations form at a high acidity. And actually, the maximum rate of nitration of these substances is reached in 95% sulphuric acid.

Thus, the active agent in the nitration of aromatic compounds is the nitronium ion. The process of nitration consists in elimination (replacement) of a proton in the unionized aromatic compound by a nitronium ion followed by binding of the eliminated proton by a base.

Ionization of aromatic compounds in too acid a medium slows down the process, while the lowering of acidity lowers the concentration of nitronium ions. These two factors are enhanced by the change in the correlation between different proton-acceptor bases owing to the change in acidity of the medium.

As a result of this, optimum acidity depends on the correlation of all three factors.

**Halogenation.** Halogenation reactions proceed according to the following scheme:

$$ArH + X|:X \longrightarrow Ar{-}X + HX$$

The active fragment attacking the aromatic ring is the halide cation. It was shown in a number of cases that the halogen cation evidently participates as a kinetically independent particle [51].

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* Practically (to avoid side reactions) nitration of phenol is carried out with dilute (20%) nitric acid in the absence of sulphuric acid. In this case, probably, the reaction proceeds through a radical mechanism, the nitrating agent being nitrogen dioxide ($\cdot NO_2$).

Thus, the rate of chlorination of sufficiently reactive aromatic compounds (of the type of phenol, anisole, etc.) by acid aqueous solutions of hypochlorous acid is independent of the concentration and of the nature of the aromatic compound:

$$v = k[\mathrm{HOCl}]$$

$$\mathrm{ArH} + \mathrm{HOCl} \xrightarrow{\mathrm{H^+}} \mathrm{Ar{-}Cl} + \mathrm{H_2O}$$

With less reactive aromatic compounds the rate depends on the concentration of the hypochlorous acid and of the aromatic compound:

$$v = k[\mathrm{HOCl}][\mathrm{ArH}]$$

A similar phenomenon, as was shown before, is observed in nitration reactions (page 506). It is apparent that the important process is that of the dissociation of HOCl to form a chlorine cation:

$$\mathrm{HOCl} + \mathrm{H^+} \rightleftarrows \mathrm{H_2O} + \mathrm{Cl^+}$$

There is no reason to believe that the active reagent is the halogen cation in all halogenation reactions.* In a number of cases the active reagent is an undissociated but polarized molecule such as $\overset{\delta+}{\mathrm{Br}}\text{—}\overset{\delta-}{\mathrm{Br}}$, which attacks the aromatic compound with its positive end. As a molecule, consisting of two different halogen atoms, has a constant dipole moment, it is not surprising, for example, that iodine chloride and iodine bromide are more vigorous agents than iodine, and that bromine chloride is more vigorous as a brominating agent than bromine:

$$\mathrm{C_6H_6} + \overset{\delta-}{\mathrm{Cl}}\text{—}\overset{\delta+}{\mathrm{I}} \longrightarrow \mathrm{C_6H_5{-}I} + \mathrm{HCl}$$

$$\mathrm{C_6H_6} + \overset{\delta-}{\mathrm{Br}}\text{—}\overset{\delta+}{\mathrm{I}} \longrightarrow \mathrm{C_6H_5{-}I} + \mathrm{HBr}$$

$$\mathrm{C_6H_6} + \overset{\delta-}{\mathrm{Cl}}\text{—}\overset{\delta+}{\mathrm{Br}} \longrightarrow \mathrm{C_6H_5{-}Br} + \mathrm{HCl}$$

It also follows from these reactions that hydrogen is replaced by the positive part of the reacting halogen molecule.

The role of catalysts accelerating halogenation (boron fluoride, ferric chloride, aluminium chloride, antimony pentachloride, tin tetrachloride, etc.) is that they promote heterolytic cleavage of the bond in the halogen molecule resulting in the formation of a halide

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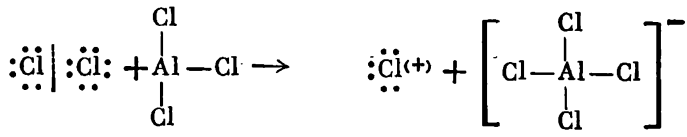
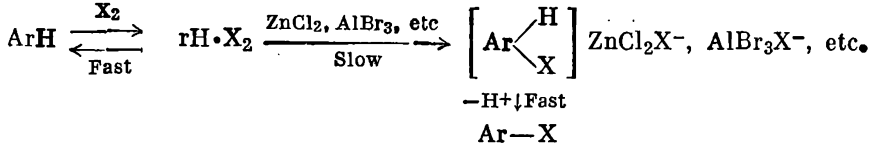
* E. A. Shilov doubts whether free halide cations play any part at all in the halogenation of organic compounds [52] in aqueous solution.

ɔation which is the active halogenating agent:



It should be remembered that halogenation of aromatic compounds ıt high temperatures may involve a radical mechanism (page 501).

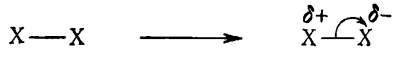
The mechanism of halogenation of aromatic hydrocarbons in the ɔresence of catalysts can be best represented at present by the fol-owing scheme:



The rate-determining step of the reaction is the simultaneous ıttack on the halogen molecule by the aromatic hydrocarbon and ɔatalyst molecules. This is confirmed by the results of kinetic inves-ıgations [53] of bromination of a large number of aromatic hydro-ɔarbons in acetic acid, catalyzed by zinc chloride: it was found hat it is a first-order reaction with respect to each of the components ArH, $X_2$ and $ZnCl_2$).

Not only metallic halides but also interhalogen compounds such ıs ICl and IBr, as well as $I_2$ and HCl, carboxylic acids and even vater catalyze this reaction [54].

All these compounds act by a similar mechanism, all of them ɔromoting polarization of the halogen molecule:



**Sulphonation.** Sulphonation of aromatic compounds is most often ccomplished by heating the compound with sulphuric acid:

$$ArH + H_2SO_4 \longrightarrow Ar{-}SO_3H + H_2O$$

Sulphur trioxide may also be employed as the sulphonating gent:

$$ArH + SO_3 \longrightarrow ArSO_3H$$

Despite the importance of sulphonation the mechanism of this eaction has not been studied sufficiently. Sulphonation is a reaction f electrophilic substitution. As is evident from a comparison of he reaction rates and activation energies listed in Table 8-14,

TABLE 8-14

**Reaction Rates and Activation Energies of Sulphonation of Benzene Derivatives***

| Compound | Sulphur trioxide | | Sulphuric acid | |
|---|---|---|---|---|
| | $K$ | $E$ (kcal/mole) | $K$ | $E$ (kcal/mole) |
| Benzene | 48.8 | 4.8 | $15.5 \times 10^{-6}$ | 7.5 |
| Toluene | — | — | $78.7 \times 10^{-6}$ | 6.8 |
| Chlorobenzene | 2.4 | 7.7 | $10.6 \times 10^{-6}$ | 8.9 |
| Bromobenzene | 2.1 | 7.8 | $9.5 \times 10^{-6}$ | 8.9 |
| Nitrobenzene | $7.8 \times 10^{-6}$ | 11.4 | $0.24 \times 10^{-6}$ | 11.0 |
| *p*-Nitrotoluene | $9.5 \times 10^{-6}$ | 11.0 | $3.3 \times 10^{-6}$ | 9.8 |

*Sulphonation was carried out in nitrobenzene at 40° [55].

electropositive substituents in the benzene ring promote and electronegative substituents inhibit sulphonation reactions. Sulphonation with sulphur trioxide takes place much faster than sulphonation with sulphuric acid.

Like in other reactions of electrophilic substitution, it is assumed that the acting sulphonating agent is the cation $^{+}SO_3H$; this assumption has been confirmed by a number of kinetic investigations.

Sulphonation with sulphur trioxide (more often used as a pyridine or a dioxane complex) is a first-order reaction with regard to the aromatic compound and a second-order reaction with regard to sulphur trioxide; the sulphonic acid formed slows the reaction down.

On the basis of these data it may be assumed that one molecule of $SO_3$ replaces the proton in the aromatic ring and a second one acts as a proton acceptor:

$$ArH + SO_3 \rightleftarrows ArH \cdot SO_3$$

$$ArH \cdot SO_3 + SO_3 \rightleftarrows ArSO_3^- + \overset{+}{S}O_3H$$

$$ArSO_3^- + \overset{+}{S}O_3H \rightleftarrows ArSO_3H + SO_3$$

Another hypothesis is that the dimer of sulphur trioxide is the effective sulphonating agent:

$$2SO_3 \rightleftarrows S_2O_6$$

$$ArH + S_2O_6 \rightleftarrows ArS_2O_6H$$

$$ArS_2O_6H \rightleftarrows ArSO_3H + SO_3$$

In any supposed sulphonation mechanism two additional peculiarities of this reaction should be considered: its reversibility and

a noticeable kinetic hydrogen-isotope effect. The latter indicates that the break of the C — H bond in the aromatic ring occurs at the stage which is the rate-determining step for the reaction as a whole [56]. Taking this into consideration, the chief mechanism of sulphonation may be expressed by the following scheme:

$$ArH + SO_3 \underset{}{\overset{\text{Fast}}{\rightleftharpoons}} \left[ \overset{+}{Ar}\begin{matrix} H \\ SO_3^- \end{matrix} \right] \overset{\text{Slow}}{\rightleftharpoons} ArSO_3^- + H^+ \overset{\text{Fast}}{\rightleftharpoons} ArSO_3H$$

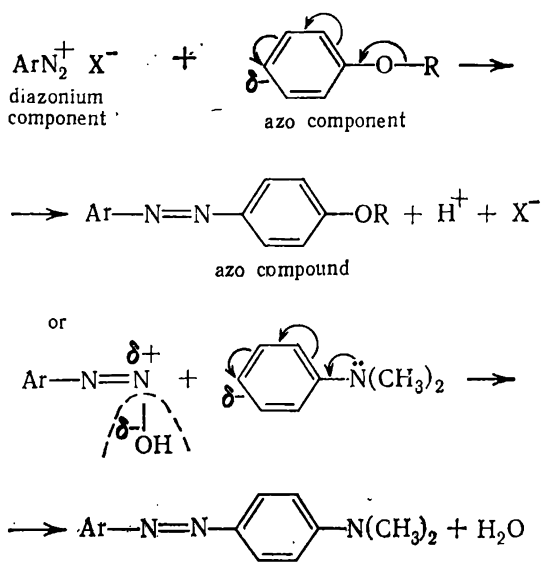
According to the isotope effect observed, the Ar — H bond is ruptured during the slow rate-determining step. The forward and back reactions of the first step are fast. There is not sufficient evidence at present to decide whether (A) is an intermediate or a transition state [57].

**Diazonium Coupling.** Amines, phenols and a few other aromatic compounds react readily with diazo compounds in buffer or alkaline aqueous solution to give azo compounds:

$$ArH + Ar'N_2X \longrightarrow Ar{-}N{=}N{-}Ar' + HX$$

This reaction is called diazonium coupling.

Diazonium coupling is an ordinary reaction of electrophilic substitution, having many things in common with nitration, halogenation and sulphonation. Its mechanism consists in the aryl diazonium cation or (which is apparently more probable in many cases) the diazo compound molecule (for instance, that of diazonium hydroxide) $Ar - N = \overset{\delta+}{N} - \overset{\delta-}{X}$ with a polarized bond N — X attacking the location of greatest electron density of an amine or phenol:

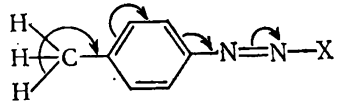


It is apparent that the ease of the diazonium coupling reactions depends on the structure of both the azo component and the diazonium component.

The greater the electron density on the carbon atom of the azo component molecule attacked by the positively charged nitrogen, the easier diazonium coupling proceeds.

Experimental data are in agreement with these assumptions. Thus, benzene derivatives containing orientants of type II, and unsubstituted benzene as well, are incapable of diazonium coupling. Substituted benzenes with strong orientants of type I, on the contrary, readily undergo diazonium coupling.

The activity of the diazo component depends on the magnitude of the partial positive charge on the nitrogen: $Ar - N = \overset{\delta+}{N} - \overset{\delta-}{X}$. If the aromatic ring of the diazo component contains a substituent of type I, this positive charge is lowered (in comparison with the unsubstituted $C_6H_5 - N = \overset{\delta+}{N} - \overset{\delta-}{X}$) and the electrophilic activity is not



high. Diazonium coupling takes place slowly.

If, conversely, the aromatic ring of the diazonium component possesses an orientant of type II, which attracts electrons, the positive charge on the nitrogen increases and the electrophilic activity of the diazo compound should be enhanced.

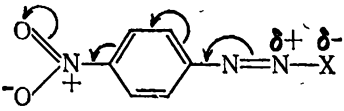


TABLE 8-15

**Dependence of Relative Rates of Coupling Reactions on Substituents in Benzene Ring of Diazo Component**

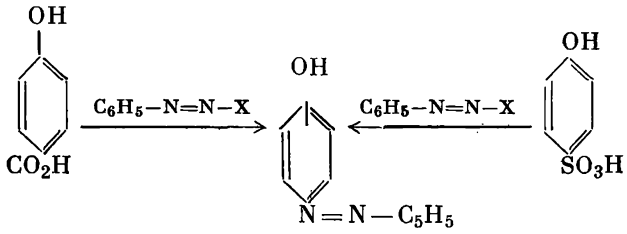
| Diazo component Ar—N=N—X | Relative rates of coupling |
|---|---|
| $C_6H_5$— | 1 |
| $p$-$O_2N-C_6H_4$— | 1,300 |
| $p$-$^-O_3SC_6H_4$— | 13 |
| $p$-$BrC_6H_4$— | 13 |
| $p$-$CH_3C_6H_4$— | 0.4 |
| $p$-$CH_3OC_6H_4$— | 0.01 |

This, for example, explains the fact that *p*-nitrophenyldiazonium salt reacts even with alkylbenzenes (e.g., with mesitylene), while phenyldiazonium salts are incapable of such reactions.

The relative reaction rates of coupling reactions depending on the substituents in the benzene ring of the diazo component are given in Table 8-15.

Diazonium coupling takes place almost entirely in the *p*-position. If the *p*-position is taken by stable substituents (of the alkyl type), the coupling occurs in the *o*-position.

Cases are known, however, where aryldiazonium salts enter into the *p*-position though it is occupied by another substituent, and this causes elimination of the substituent:




**Alkylation *.** Alkylation of aromatic hydrocarbons is effected by the action of alkyl halides, alcohols, ethers, esters and catalysts (aluminium chloride, stannic chloride, boron trifluoride, sulphuric acid and others), on aromatic compounds

$$ArH + AlkX \xrightarrow{\text{catalyst}} Ar-Alk + HX (X = Cl,\ OH,\ OAlk,\ RCOO)$$

Alkylation is a reaction of electrophilic substitution. The function of the catalyst consists in breaking off the anion to form a reactive cation. For example:

$$Alk|:X + AlCl_3 \longrightarrow Alk^+ + AlXCl_3^-$$

$$Alk^+ + ArH \longrightarrow Ar-Alk + H^+$$

This idea of the role of catalysts, at least in the case of alkyl halides, is borne out by a number of experimental facts.

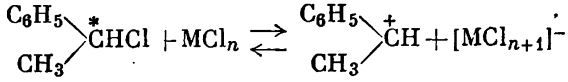
Thus, solutions of aluminium halides in alkyl halides conduct electric current, indicating the presence of ions in such solutions. If in the alkylation of benzene an alkyl halide and an aluminium halide, containing different halogen atoms are used, a mixture of hydrogen halides results [59].

Furthermore, alkylation of benzene with benzyl chloride in the presence of aluminium bromide results in a mixture of 25.67% hydrogen chloride and 74.33% hydrogen bromide.

* For review on Friedel-Crafts reaction see [58].

If benzene is alkylated by benzyl bromide in the presence of aluminium chloride, a mixture of 79.41% hydrogen chloride and 20.59% hydrogen bromide results.

Optically active alkyl halides are racemized under the influence of catalysts of alkylation reactions:

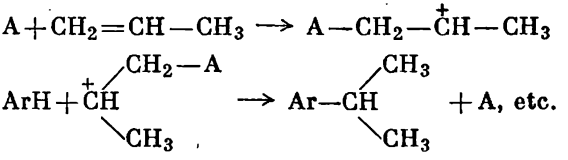


The rate of racemization decreases, when catalysts are substituted for one another, in the following sequence:

$$SbCl_5 > SnCl_4 > TiCl_4 > BCl_3 > ZnCl_2 > HgCl_2$$

It should not be thought that a free alkyl cation participates in all reactions of this type. A complex of the type $\overset{\delta+}{Alk}\cdots\cdots X \cdots\cdots \cdots\cdots \overset{\delta-}{AlCl_3}$ in which the C — X bond is polarized rather than broken may also be the alkylating agent.

In the alkylation of aromatic hydrocarbons by alkenes the catalyst adds first to the alkene; the resulting cation attacks the aromatic ring:



Like other reactions of electrophilic substitution, alkylation proceeds in accordance with the rules of orientation; in the alkylation of benzene *o*- and *p*-dialkylbenzenes are formed.*

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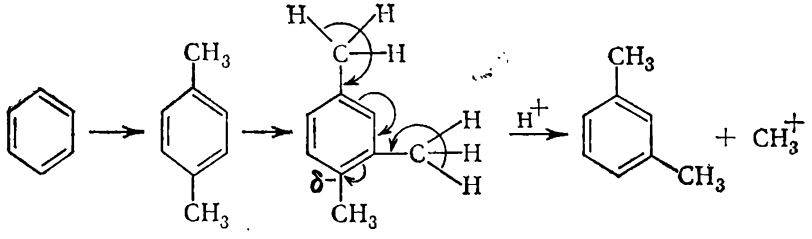
* The predominant formation of *m*-dialkylbenzenes observed in some cases when reaction is carried out at an elevated temperature (50-100°) is due to the fact that alkylation is a reversible reaction, and dealkylation of trialkylbenzenes results in *m*-dialkylbenzenes:

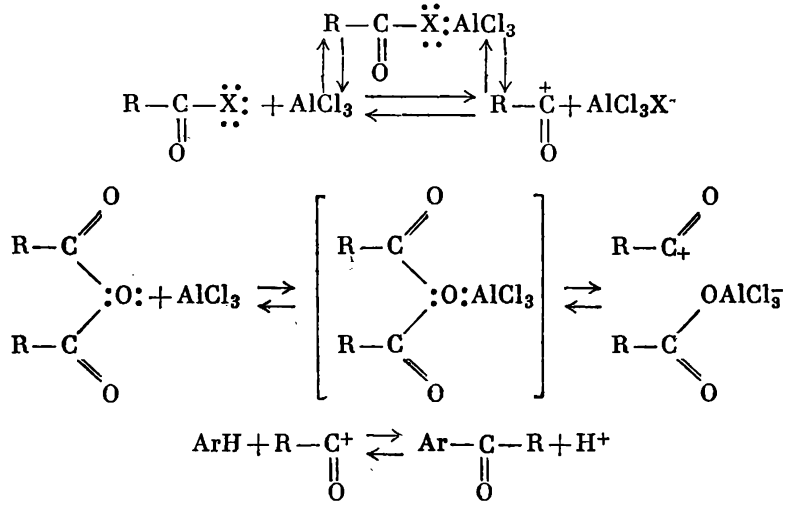


As carbonium ions are formed during alkylation reactions, it is natural that isomerization occurs in a number of cases (see page 550 *et seq.*).

**Acylation.** Acylation proceeds similarly, in principle, toalkylation:

$$ArH + RCOX \xrightarrow{AlCl_3} ArCOR + HX$$

Acylation reactions are most commonly accomplished with acid halides and with aluminium chloride as the catalyst. Acid anhydrides may be employed instead of acid chlorides. The reaction mechanism is alike in both cases.



The above scheme presents the reaction mechanism in somewhat simplified form, because actually the oxygen atoms of the carbonyl groups (in the acid chlorides and anhydrides) are apparently also coordinationally linked to the aluminium chloride in the course of the reaction.

It should be noted that for the acylation of sufficiently reactive substances the complex $R-\overset{\displaystyle O}{\overset{\|}{C}}-\ddot{\underset{\ddot{}}{Cl}}:A$ (A being a Lewis acid) may serve as the acylating agent without preliminary dissociation into $R\overset{+}{C}O$ and $ClA^-$ ions. For example [60], anisole is acylated in the presence of iodine almost exclusively with the $R-\overset{\displaystyle O}{\overset{\|}{C}}-Cl:I_2$

omplex and not with the ionic pair $R\overset{+}{C} = O/\overset{+}{C}lI_2^-$, because in such ases the anion $ClI_2^-$ is very unstable.

**Mercuration.** Mercuration, which is of much less practical significance than the electrophilic substitutions discussed above, proceeds as follows:

$$ArH + HgX_2 \longrightarrow Ar—HgX + HX$$

It has been known for a long time that mercuration of aromatic compounds is independent of the nature of the substituent in the ring and that it takes place predominantly in the *ortho-* and *para*-position. For example, mercuration of nitrobenzene results predominantly in the *o*-isomer, a small amount of the *p*-mercurated product and up to 40% of the *m*-derivative. In the mercuration of benzoic acid and its methyl ester mercury enters exclusively ortho to the carboxyl.

These facts may be regarded as evidence in favour of a radical mechanism for mercuration reactions.

It was shown in 1950 [61], that many of the apparent anomalies of orientation in the mercuration of aromatic compounds become easier to understand if mercuration by ionized mercuric salts in solutions of strong acids is considered separately from mercuration by weakly dissociated mercuric acetate in nonpolar solvents.

In the first case, for instance, in mercuration by mercuric perchlorate in an aqueous solution of chloric acid, the usual orientation for electrophilic substitution is observed, as is shown by the data on mercuration of nitrobenzene, given in Table 8-16.

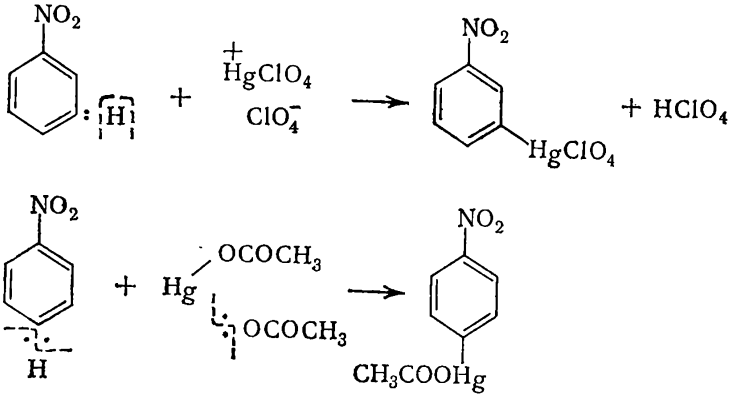
TABLE 8-16

**Mercuration of Nitrobenzene**

| Conditions of experiment | Temperature | % *ortho-* and *para-* isomers | % *meta-* isomers |
|---|---|---|---|
| $Hg(ClO_4)_2$ in 60% $HClO_4$ | 23° | 11 | 89 |
| $Hg(ClO_4)_2$ in 40% $HClO_4$ | 95° | 37 | 63 |
| $Hg(CH_3COO)_2$ in excess of $C_6H_5NO_2$ | 95° | 52 | 48 |
| $Hg(CH_3COO)_2$ in excess of $C_6H_5NO_2$ | 150° | 57 | 43 |

When nitrobenzene is mercurated with mercuric acetate, the orienting effect is much less pronounced, this being one of the indications of a homolytic process.

Thus, mercuration of aromatic compounds may follow either an ionic or a radical mechanism, depending on the reaction conditions:

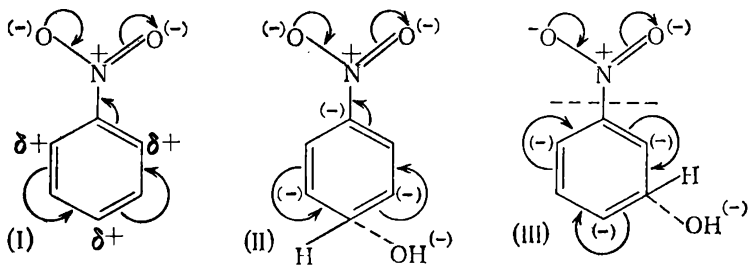



## 8-3.5 Nucleophilic Substitution in the Benzene Ring

In nucleophilic substitution the aromatic compound is attacked by a reagent which may be either an anion, or a neutral molecule with a constant dipole or one that arises at the moment of reaction, the active centre being the negative end of the molecule, possessing a free electron pair, as in ammonia, etc.

The relationships in this case are naturally opposite to those observed in electrophilic substitution.

Let us consider, for instance, the hydroxylation of nitrobenzene. Here approach of the nucleophilic hydroxyl anion to the *o*- and *p*-positions of nitrobenzene is facilitated owing to the presence in these positions of effective positive charges.




Unreacted molecule | Attack on the p-position | Attack on the m-position

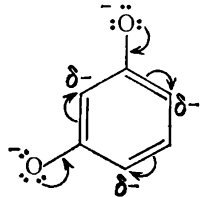
Besides, in transition state II, which arises when the hydroxyl ion attacks the *o*- or *p*-position, the substituent participates in delocalization of the negative charge. When the *m*-position is attacked, transition state III arises, in which the negative charge is more localized, because owing to structural peculiarities the substi-

tuent cannot participate in delocalization of the negative charge. The unfavourable distribution of effective charges (the nitrogen and the carbon bound with it carry equal charges) must also increase the energy of state III. Thus, both static and dynamic factors favour *o*-, *p*-substitution.

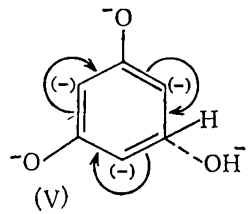
Because of this the nitro group and other electronegative substituents are *ortho-para*-orientants in nucleophilic substitution.

Since nucleophilic reagents attack the points of lowest electron density, it is natural that nucleophilic substitution should proceed with greater difficulty in unsubstituted benzene than in nitrobenzene or in any other substituted benzene containing a substituent of type II. Nucleophilic substitutions in benzene derivatives containing a substituent of type I are very rare and generally require forced conditions.

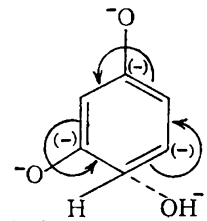
Take, for instance, the reaction of hydroxylation of resorcinol. As the reaction proceeds in an excess of caustic, the resorcinol ion actually reacts with the hydroxyl ion:



(IV)
Unreacted molecule



(V)
Attack on the m-position



(VI)
Attack on the o-(p)-position

Approach of the hydroxyl ion to the benzene ring of the resorcinol ion which has a higher electron density (IV) is difficult. Approach to the *o*- and *p*-carbon atoms is especially difficult.

The attack of the hydroxyl ion on the *o*-, *p*-position gives rise to a transition state (VI), the attainment of which requires greater energy than when the *m*-position is attacked (V) because of the unfavourable distribution of effective charges in state (VI) (both oxygens and the carbon atoms bound to them carry like charges).

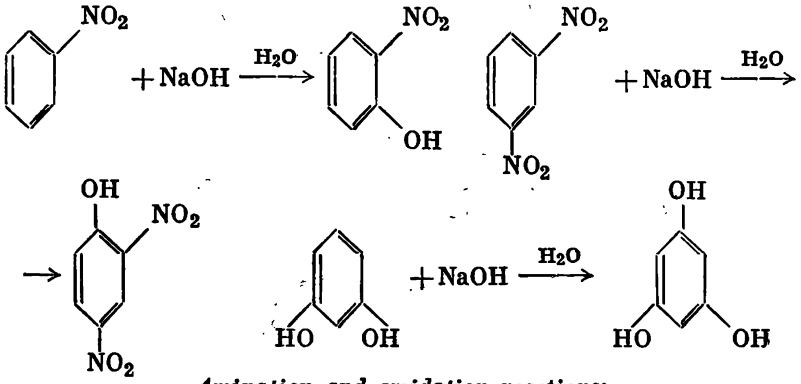
Thus, the combined influence of static and dynamic factors results in *meta*-substitution if the benzene ring contains electron-donor substituents (hydroxyl, amino group, etc.).

The fate of the substituted hydrogen atom varies depending on the actual nature of the reaction. Its removal often depends on the presence of electron-acceptor molecules (e.g., oxygen), sometimes it is eliminated as molecular hydrogen or as a metal hydride (i.e., $H^-$).

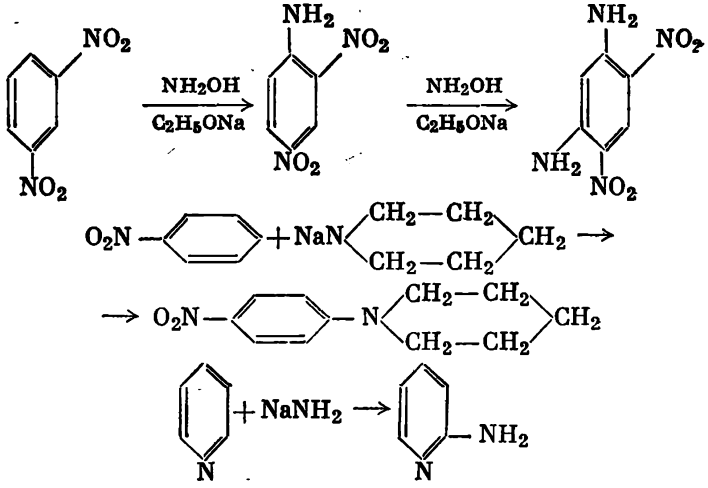
As nucleophilic substitution reactions are of less practical importance than those of electrophilic substitution they have not been studied so extensively. However, theoretically they are just as important.

Below are given examples of nucleophilic substitution reactions.

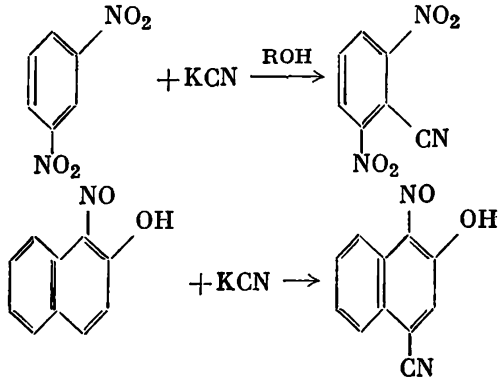
*Hydroxylation reactions*:



*Amination and amidation reactions*:

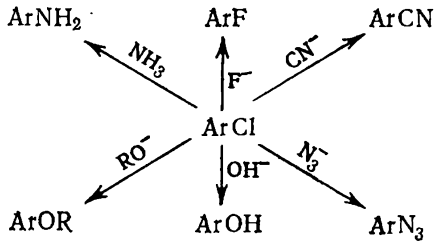


*Cyanidation reaction*:



Besides nucleophilic replacement of hydrogen by hydroxyl, amino and cyano groups, a fairly larger number of reactions are known where an atom or group of atoms other than hydrogen is replaced.

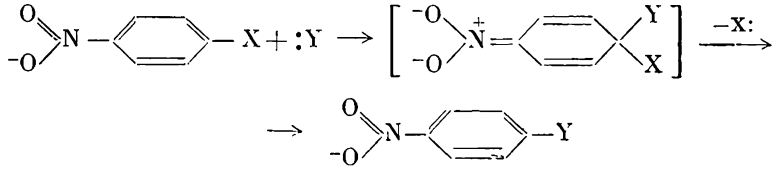
The most extensively studied are reactions of replacement of a halogen by nucleophilic reagents:




Generally reactions of this type proceed only under drastic conditions, but if there are electron-attracting groups (in the *o*- or *p*-positions with respect to the halogen atom) the halogen becomes more reactive.

### Bimolecular Mechanism

Nucleophilic substitution reactions in the aromatic series of the type of hydrolysis of *ortho*- and *para*-nitrochlorobenzenes proceed according to a bimolecular mechanism.

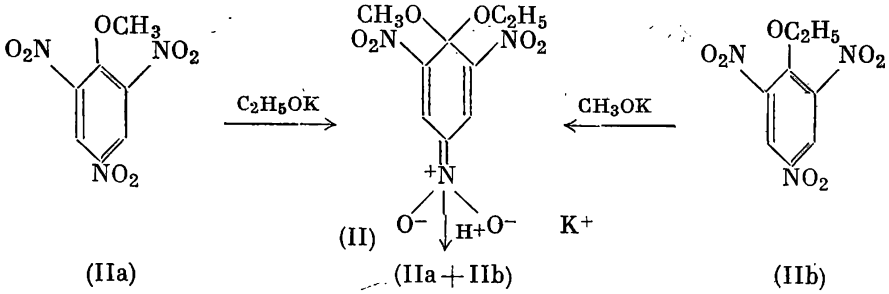


Kinetically these are second-order reactions. The question is whether (I) is an unstable intermediate or an activated complex in an $S_N2$ reaction.

The preparation of salts with anions apparently analogous to structure (I) shows that in certain (and possibly in all) cases structure (I) is an intermediate compound.

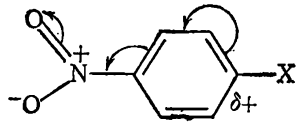
The commonest salt of this type is salt II, formed by the action of potassium ethylate on 2,4,6-trinitroanisole (IIa). As Meisenheimer [61a] showed, this salt is evidently identical with that formed under analogous conditions from potassium methylate and 2,4,6-trinitrophenetole (IIb) (when acidified salt II gives the same mixture

nitroethers, no matter which of these two ways it is obtained).




(IIa) (II) (IIa + IIb) (IIb)

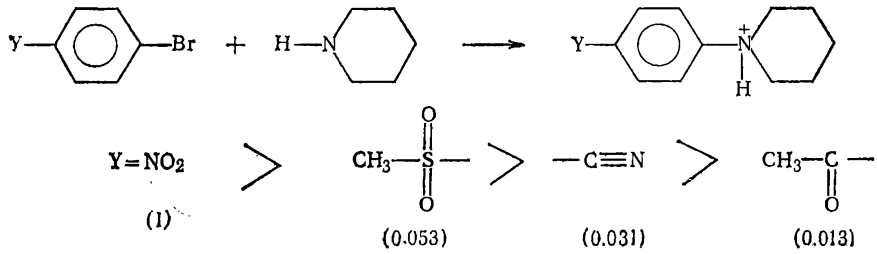
The reason for the increase in reactivity of halo-substituted compounds in $S_N2$ reactions under the influence of electronegative groups is that the II type substituent, for example, the nitro group, increases the positive effective charge on the carbon atom linked with the halogen by drawing electrons away mainly from the *o*- and *p*-carbon atoms:




This facilitates attack on the carbon atom by a nucleophilic reagent, say, by a hydroxyl ion.

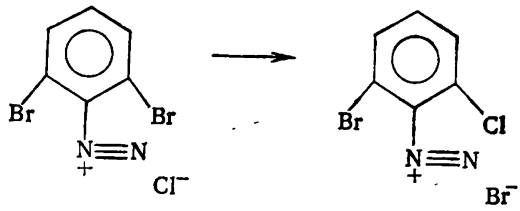
The nitro group, which is the strongest orientant of the II type, activates $S_N2$ reactions in the aromatic series much more than weaker electronegative groups such as the nitrile or acetyl groups.

By way of comparison, the relative rates of the reaction of *para*-substituted bromobenzenes with piperidine are given below (the reaction rate of *p*-nitrobromobenzene being taken as unity) [62]:

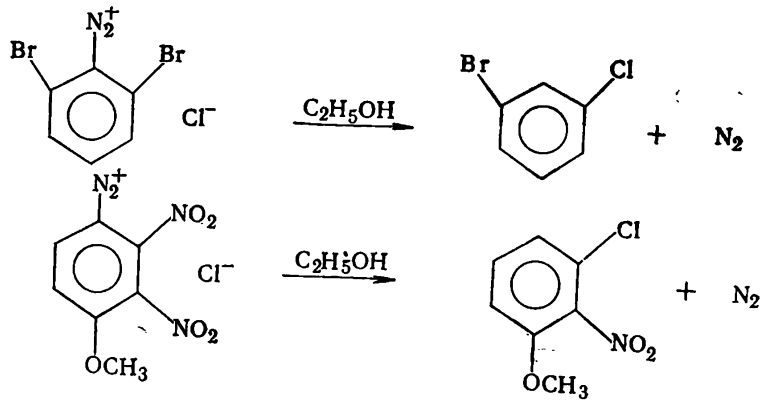



The diazonium group has a very strong activating effect on the reactivity of halides. Thus, chlorides of 2,4-dibromo- and 2,6-dibromophenyldiazonium salts are converted into bromochloro-

phenyldiazonium bromides even at room temperature in alcoholic solution, e.g.:

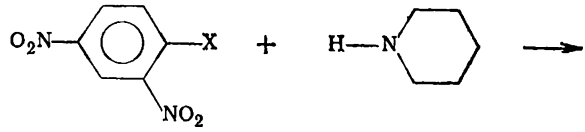


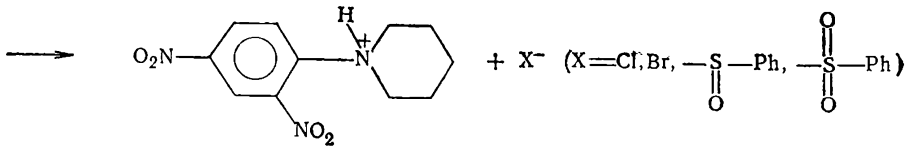
This type of exchange may involve elimination of nitrogen:



It should be also noted that the rate of bimolecular nucleophilic substitution of Ar — X does not depend on the nature of the substituent X.

Thus, in studying the kinetics of reactions of 2,4-dinitro compounds with piperidine [63]





it was discovered that dinitro compounds contaning the substituents Cl, Br and —SOPh react at about the same rate; the compound

ntaining the substituent $-SO_2Ph$ reacts 67 per cent faster. Of urse, if rupture of the C — X bond were of great signifi- nce (as in monomolecular reactions) one would expect a much eater difference between the rates of the reactions in ques- on.

The activation energies of the reactions of all four compounds e approximately the same, shownig that the nature of the activa- on process is the same irrespective of the substituent X. Thus, molecular nucleophilic substitution reactions in the aromatic ries have the following characteristic features:

(1) They are kinetically second-order.

(2) Electron-acceptor substituents located in the *ortho-* and *para-* ositions accelerate the reaction.

(3) Substitution is easier under the action of strongly nucleophilic agents.

(4) The reaction rate is essentially independent of the nature of e substituent X.

### Monomolecular Mechanism

In some cases nucleophilic substitution reactions in the aromatic ries follow a monomolecular mechanism. Such is the decomposi- on of aryldiazonium cations. The decomposition of phenyldiazo- um chlorides in water is a first-order reaction [64]; the rate of the action (not counting the salt effect and solvent effect) remains nchanged when alcohol or chloride anion is added.

The slow rate-determining step is the rupture of the carbon- trogen bond in the aryldiazonium cation

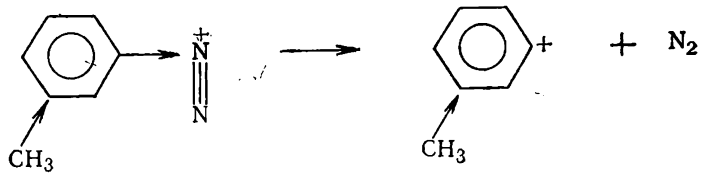
$$Ar-\overset{+}{N}\equiv N \xrightarrow{\text{Slow}} \overset{+}{Ar} + N_2$$

the second, fast stage the aryl cation reacts with the nucleo- ilic reagent, forming the end product:

$$Ar-\begin{cases} \xrightarrow{HOH} Ar-OH + H^+ \\ \xrightarrow{ROH} Ar-OR + H^+ \\ \xrightarrow{Cl^-} Ar-Cl \end{cases}$$

Obviously, decomposition of the aryldiazonium cation into the yl cation and nitrogen should be facilitated by electron-donor

substituents, e.g.:



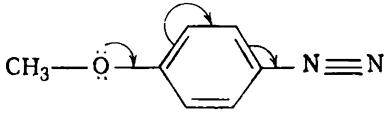
In this case not only is the heterolytic cleavage of the C:N bond facilitated, but a more stable aryl cation (compared to phenyl) is formed.

It is clear, therefore, why electronegative substituents, as a rule, slow down, and electropositive substituents accelerate the decomposition of aryldiazonium salts. The relative rates of decomposition of substituted aryl-diazonium chlorides $XC_6H_4N_2Cl$ (in water at 29°) [65] have the following values:

$$X = p\text{-}O_2N < m\text{-}Cl < H < m\text{-}CH_3 < m\text{-}OH$$
$$(1/240) \qquad (1/24)\ (1) \qquad (4.5) \qquad (12)$$

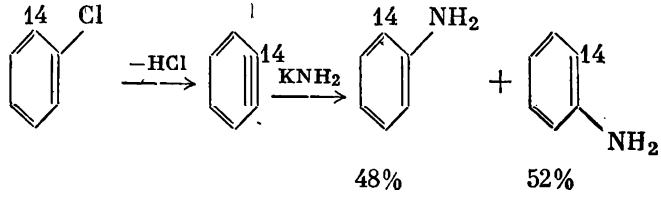
But it is rather difficult to explain why the $p$-OH and $p$-$CH_3$ — O groups greatly retard the rate of decomposition of diazonium salts.

Possibly, in these cases, the electron density of the C — N bond is enhanced owing to conjugation and it becomes more stable.



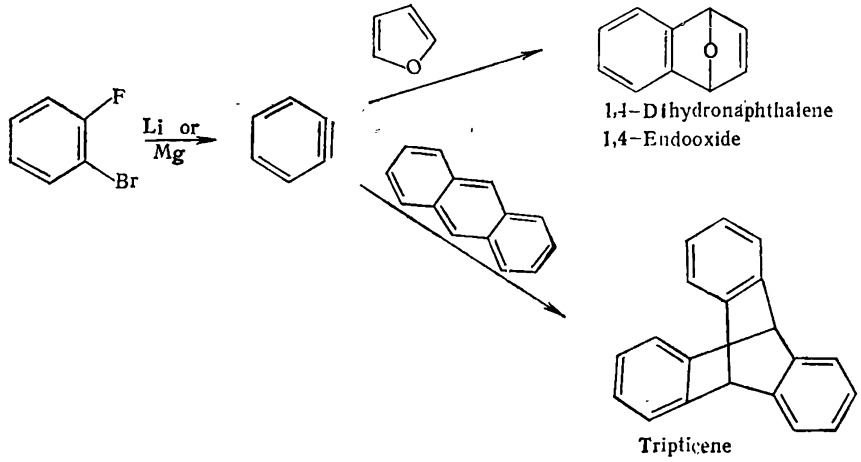
**Nucleophilic Substitutions Passing Through the Stage of Formation of Dehydrobenzene (Cyclohexadienyne, Benzyne)**

In 1959 Roberts and coworkers [66] established that when potassium amide reacts with phenyl chloride labeled with $C^{14}$ equal amounts of anilines labeled in positions 1 and 2 result. From the results obtained Roberts drew the conclusion that hydrogen chloride is first eliminated from the chlorobenzene to form *dehydrobenzene* ("aryne" as the authors called it). After this a molecule of potassium amide adds to the triple bond of this compound:



Wittig, who suggested as far back as 1940 [67] that dehydrobenzene orms as an intermediate in certain reactions, later discovered number of interesting reactions, which in a certain sense might be onsidered identification of dehydrobenzene.

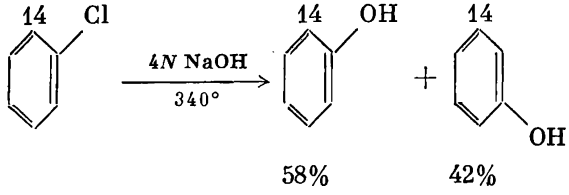
For example, in the reaction of *o*-fluorobenzene with lithium or iagnesium in the presence of furan an adduct of dehydrobenzene ınd furan is formed, namely the 1,4-endooxide of 1,4-dihydrona-hthalene [68]. The presence of anthracene gives rise to triptycene [69].




Dehydrobenzene forms as an intermediate in those cases of nu-leophilic substitution where the halogen in the benzene ring is ot activated by an electronegative substituent (e.g., by an *ortho-* r *para*-nitro group) and the reaction itself proceeds under drastic onditions.

It has been proved, for instance, that the commercial synthesis f phenol from chlorobenzene also passes through a dehydrobenzene tage [70, 71].

This follows, in particular, from the results of a study of chloro-enzene labeled with $C^{14}$ [70]:




Hydrolysis of any of the three isomeric chlorotoluenes results in ıe same mixture of cresols [72]. Evidently in this case also the ıaction proceeds through a common intermediate—dehydrotoluene.

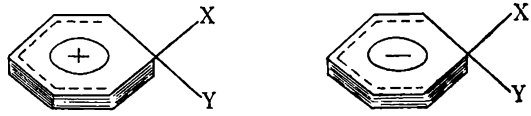
The hydrolysis of isomeric *o*-, *m*-, and *p*-chlorophenols in alkaline solution, which results in resorcinol exclusively in all these cases, can be explained by the formation of aryne intermediates. Probably, the formation of resorcinol in the caustic fusion of *m*- and *p*-benzenedisulphonic acids is also due to a similar mechanism.

It should be kept in mind that dehydrobenzene has neither been isolated to date nor has its existence been proved directly by physical methods. All the proofs have been indirect.

In conclusion it should be noted that the sphere of reactions involving the intermediate formation of dehydrobenzene is quite limited. It is the sphere of nucleophilic substitution proceeding under drastic conditions, where the molecules of the reacting substances do not possess activating groups such as $NO_2$.

### 8-3.6 Steric Factors. Orientation in the Benzene Ring and Coplanarity of Molecules

The stereochemistry of substitution reactions at an aromatic carbon atom cannot be studied by the methods employed for tetrahedral and alkene carbon atoms. Nevertheless it may be assumed that on nucleophilic and electrophilic substitution in the benzene ring the activated complexes I and II have the following structures:




(I) (II)

The configuration of the carbon atom serving as the reaction centre is close to tetrahedral [73, 74].

In the case of free-radical substitution our knowledge is much more meagre and no general model of the intermediate state can therefore be proposed.

It was indicated above (page 469) that one of the structural features of an aromatic molecule is its coplanarity and consequently parallelism of its π-electron axes.

Coplanarity is also a necessary condition for the orienting influence of substituents possessing *p*-electrons on the benzene ring during electrophilic and nucleophilic substitutions.*

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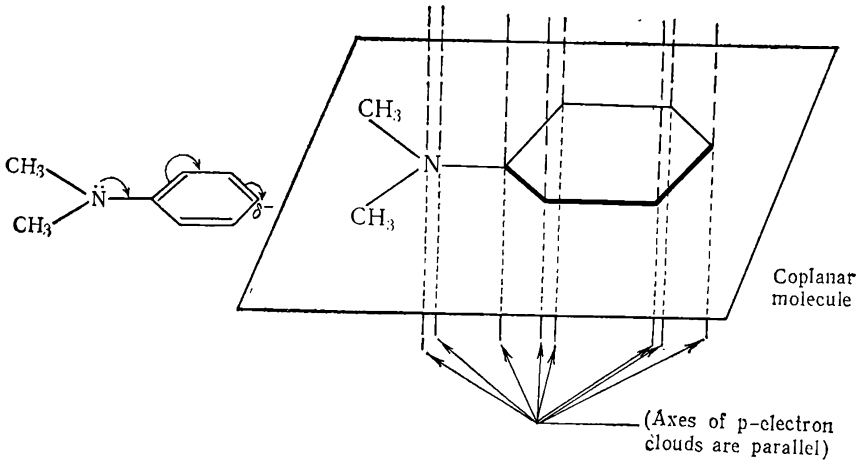
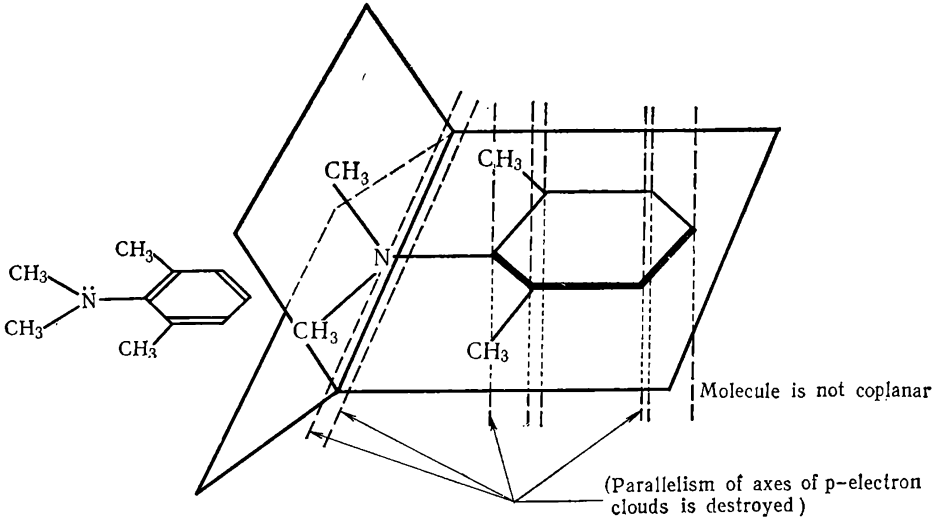
* The question of radical substitution has not been studied.

The high reactivity of the *p*-position of dimethylaniline with regard to electrophilic reagents is well known:




If, however, two methyl groups are introduced into the *ortho*-position to the dimethylamino group, such a dimethylxylidine will react no longer with nitrous acid, diazo compounds or aldehydes.

In the flat dimethylaniline molecule nothing prevents the axes of the *p*-electron clouds at the nitrogen atom from assuming a position parallel to the axes of the π-electron clouds of the benzene ring. In the dimethylxylidine molecule the *ortho*-methyl groups prevent the molecule from being flat and consequently destroy the

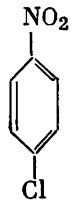


parallelism of the axes of nitrogen *p*-electrons with those of the benzene ring. The orienting action of the dimethylamino group is thus cancelled and the benzene ring becomes incapable of nitrosation, diazonium coupling and similar reactions, just as is the case in unsubstituted benzene.

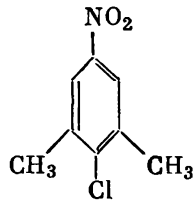
It is known that the chlorine atom in the benzene ring is not very mobile in nucleophilic substitution reactions, and that a nitro group in the *o*- or *p*-position increases its mobility.

However steric hindrances which destroy coplanarity and cancel the effect of the nitro group may change this picture substantially.

For example, in the molecules of chloronitrobenzene (I) and chloronitroxylene (II) nothing prevents the nitro group from arranging itself in the same plane as the benzene ring:

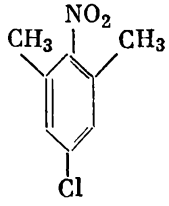



(I)

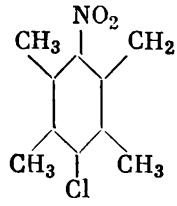



(II)

The chlorine is mobile in both compounds owing to the influence of the nitro groups. In isomeric chloronitroxylene (III) and in chloronitrodurene (IV) the nitro group is ousted from the plane of the benzene ring by the two neighbouring methyl groups:




(III)



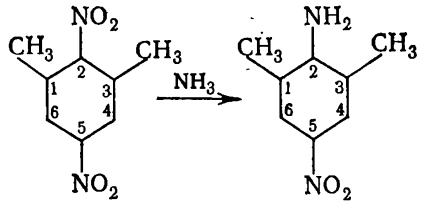

(IV)

Here the nitro groups exert no influence and the chlorine is no more mobile than in chlorobenzene.

Destruction of coplanarity of the molecule owing to steric hindrances and the attendant elimination of the orienting action of substituents sometimes leads to rather interesting, at first glance, anomalous results.

Thus if 2,5-dinitro-*m*-xylene (V) is heated with aqueous ammonia in a sealed tube, a nitro group in position 2 is replaced by an amino group forming nitro-

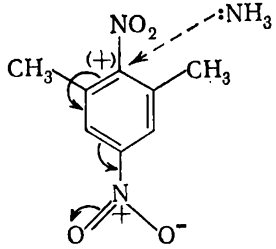
ιylidine (VI):




(V) (VI)

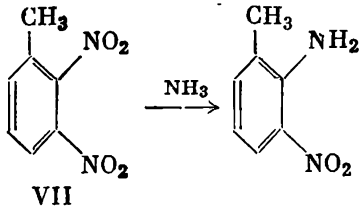
It would seem that the nitro group in position *5* should be replaced, because hat in position *2* is sterically blocked by two *o*-methyl groups. Besides, methyl groups should exert a deactivating influence on the *o*-position in nucleophilic ubstitution.

However, if it is taken into account that the nitro group in position *5* is n the plane of the benzene ring while that in position *2* is outside of this plane verything can be understood. The orienting influence of the latter nitro group s cancelled while the nitro group in position *5* activates substitution in the *p*-osition inducing a positive charge on the *p*-carbon atom:

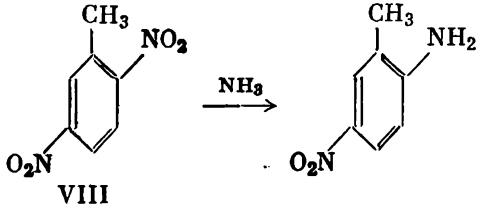



As a result of this nucleophilic substitution occurs at position *2*.

For similar reasons in 2,3-dinitrotoluene (VII) and in 2,5-dinitrotoluene VIII) aqueous ammonia substitutes for nitro groups predominantly in position *2*.




VII



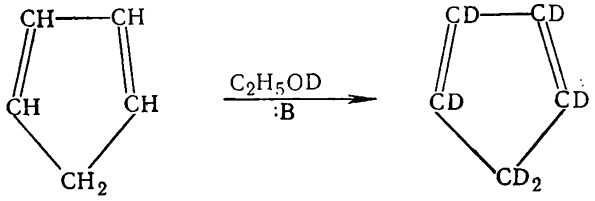

VIII

In both reactions the substituted group is in the *o*- or *p*-position to the nitro roup experiencing less hindrance to arrangement in the plane of the benzene ng.

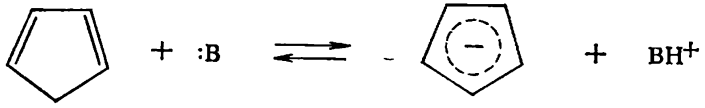
## 8-3.7 Reactivity of Non-Benzenoid Aromatic Compounds

### Cyclopentadienyl Anion

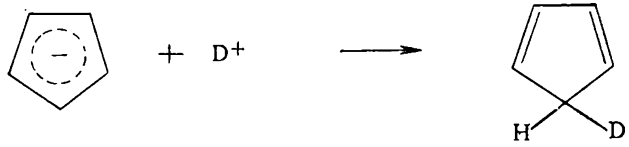
Cyclopentadiene very readily exchanges all of its six hydrogen atoms when treated with deuteroethanol in alkaline solution [75].




This phenomenon is due to the initial formation of a cyclopentadienyl anion under the influence of the base.



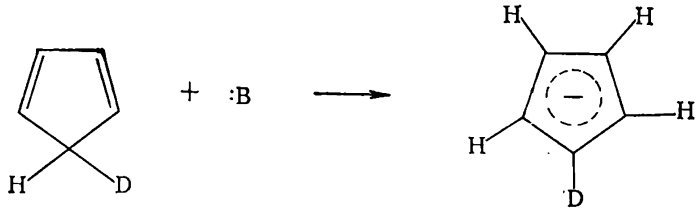

Deuteron adds easily to the cyclopentadienyl ion forming a deuterium-containing cyclopentadiene



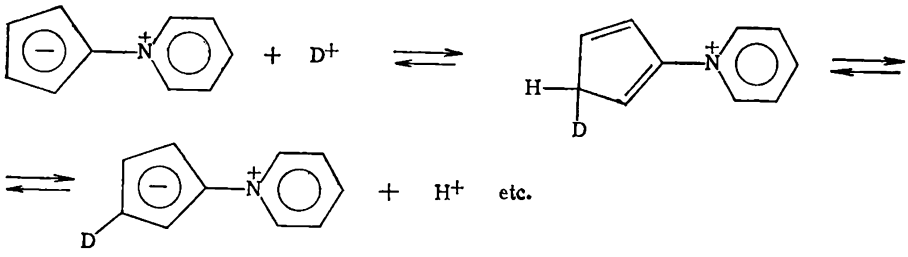

The latter loses a proton to the base forming a deuterated cyclopentadienyl anion.

Repetition of these two reactions eventually results in complete exchange of hydrogen for deuterium in cyclopentadiene. This reaction is a good chemical confirmation of the equivalence of all the carbon atoms in the cyclopentadienyl anion.

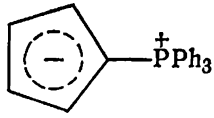
Cyclopentadiene does not enter into the deuterium exchange reaction in neutral or weakly acidic solutions, because formation of the cyclopentadienyl anion is impossible under these conditions.



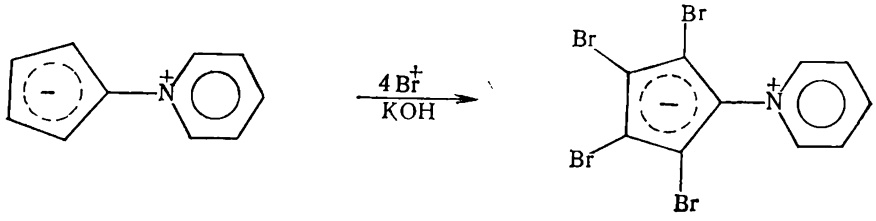
In ylide molecules where the cyclopentadienyl anion is a part of the molecule, deuterium-hydrogen exchange takes place in the five-membered ring not only in alkaline, but in neutral and weakly acidic solution as well [76].




Triphenylphosphoniumcyclopentadienylide enters into deutero exchange reactions just as easily.



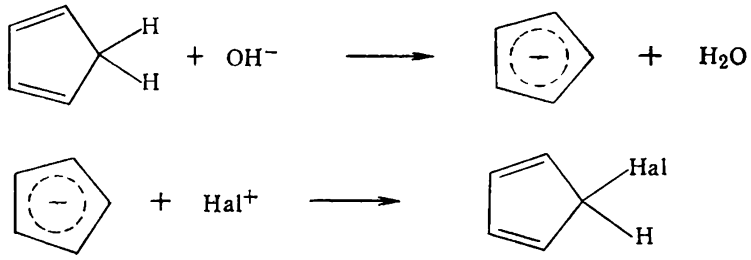

The ease with which electrophilic reagents attack the cyclopentadienyl ring of ylides is illustrated by the reaction of pyridinecyclopentadienylide with alkaline solution of potassium hypobromide.




All four hydrogen atoms are replaced by bromine atoms [76]. It should be noted that cyclopentadiene also exchanges all its hydrogen atoms for halogens when treated with alkaline solutions of hypochlorous and hypobromous acids [77].

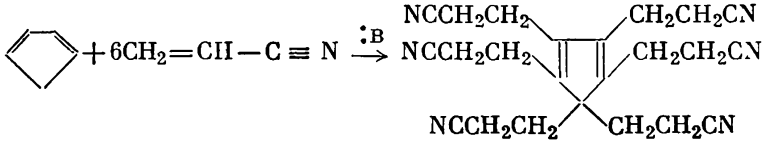
In this case, probably, the first step of the reaction is the formation of the cyclopentadienyl anion, which is then attacked by a positively charged halogen cation resulting in the formation of mono-

substituted cyclopentadiene:



Halogen-substituted cyclopentadiene reacts with the alkali forming a halogen-substituted cyclopentadienyl anion. The latter is attacked by halogen again. Repetition of these reactions results in the formation of hexahalo-substituted cyclopentadienes.

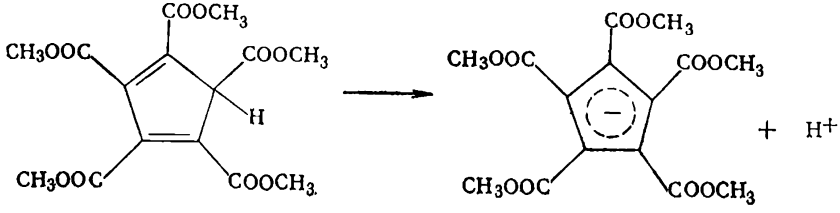
The reaction of cyclopentadiene with acrylonitrile (in dioxane at 20° in the presence of a base) resulting in the formation of hexa-(2-cyanoethyl)-cyclopentadiene [78] proceeds in a similar way:



The examples cited above show that cyclopentadienyl ion reacts readily with electrophilic reagents. It should also be noted that cyclopentadiene sulphonates readily with pyridine-sulphur trioxide, mercurates with mercuric chloride in methanol, and couples with diazotized 2,4-dinitroaniline.

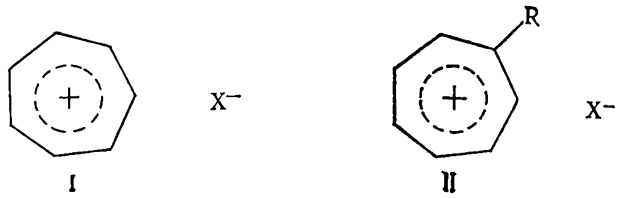
Owing to the great tendency of cyclopentadienyl anion to react with electrophilic reagents, it cannot be obtained in high concentrations in protic solvents such as water or alcohol, because it removes protons from the solvent molecules forming cyclopentadiene. However, as was mentioned before, the cyclopentadienyl ion can exist in stabilized form in ylide molecules.

The stability of the cyclopentadienyl anion increases as the hydrogen atoms of the five-membered ring are exchanged for electron-attracting groups. For example, substance (I) is a stronger acid than hypochloric acid because when (I) dissociates an extremely stable ion (II) is formed [79].



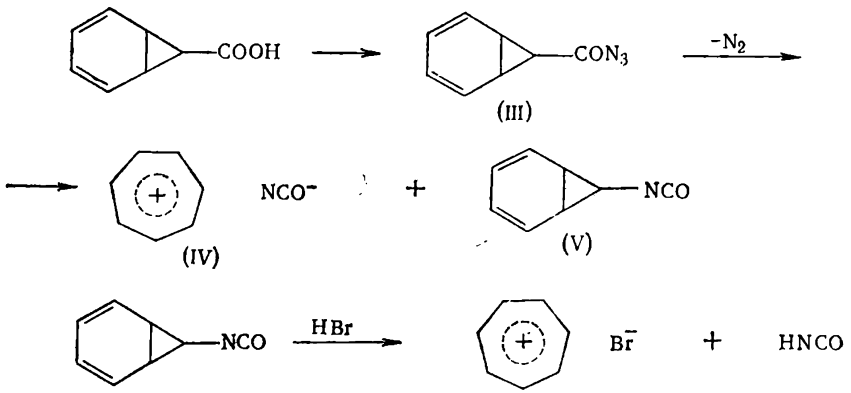
### Tropylium Cation

Several methods of obtaining the seven-membered aromatic tropylium system are known.




I II

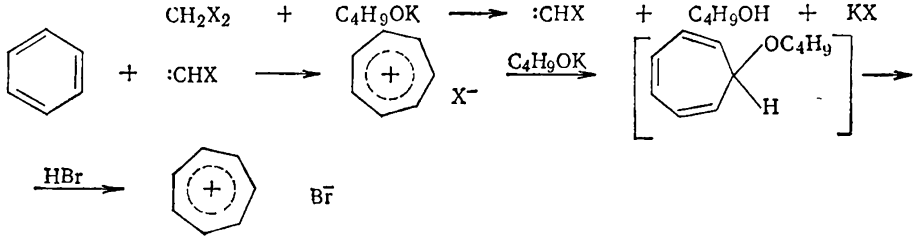
Tropylium bromide was first prepared by Doering and Knox in 1954 by the elimination of hydrogen bromide from dibromocycloheptadiene. Later a method was worked out based on the ready isomerization of the norcaradiene system. In the Curtius rearrangement of norcaradiene carboxylic acid (III) tropylium isocyanate (IV) results together with the covalent cyanate (V), which can be converted into tropylium bromide by the action of hydrogen bromide [80]:




A number of methods of synthesizing tropylium compounds are based on the fact that cycloheptatriene (tropylidene) readily eliminates a hydride ion to form the stable tropylium system. Various Lewis acids can be used for eliminating the hydride ion [81] ($H_2SO_4$, $AlCl_3$, $PCl_5$).

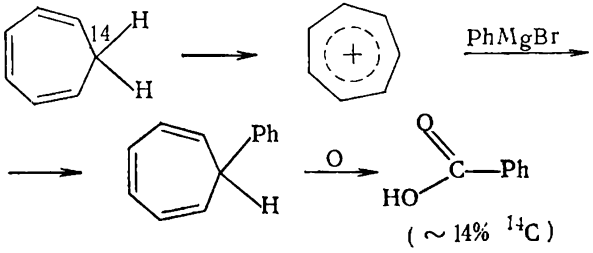
In the synthesis of tropylium salts it is convenient to use the reaction of heptacyclotriene and triphenylmethyl halides in highly ionizing solvents [82]:

Recently tropylium has been obtained by the reaction of monohalo carbenes with benzene [83]. In the reaction of potassium *tert*-butoxide with $CH_2Cl_2$, $CH_2Br_2$, $CH_2I_2$ in benzene solution, followed by treatment with hydrogen bromide, small amounts of tropylium bromide are always formed




The equivalence of all the carbon atoms in the tropylium cation was proved as follows [84].

Cycloheptatriene labeled with $C^{14}$ in the methylene link by two different methods (by addition of $Br_2$ followed by elimination of 2HBr and by the action of $PCl_5$) was converted into tropylium bromide. Tropylium bromide was treated with phenylmagnesium bromide. The resulting phenyltropylidine was oxidized to benzoic acid. It was established that the benzoic acid contained 1/7 of the initial $C^{14}$ (in its carboxylic group) within the experimental error.

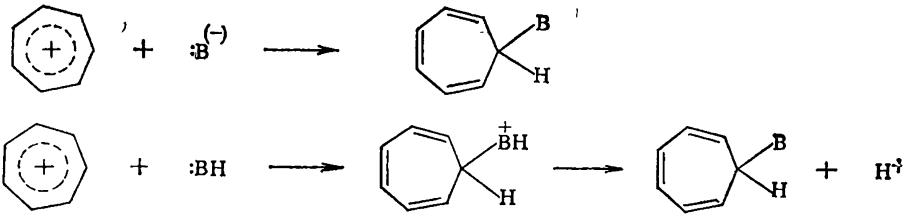



**Reactions of Tropylium Salts with Nucleophilic Reagents**

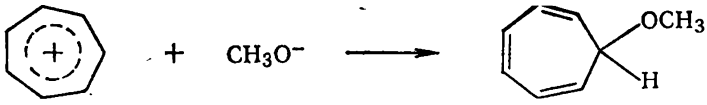
Tropylium ion, unlike most other carbonium ions, is quite stable, its reactions can be studied directly and may to a certain extent serve as convenient reaction models of carbonium ion in general.

The most important property of tropylium ions, as of other carbonium ions, is its electrophilic nature, that is, ability to react

ith nucleophilic reagents according to the following scheme:



For example, the reaction of sodium methoxide with tropylium lts results in 7-methoxytropylidene, and if these salts are acted n by potassium cyanide, 7-cyanotropylidene is formed [85, 86]:



Tropylium salts are quite active in alkylation reactions of com- ounds containing mobile hydrogen atoms [87].

Thus, malonic acid, acetoacetic ester, cyanoacetic ester and troacetic ester react rapidly with tropylium salts at room temper- ure. In all cases corresponding substitution products of the cyclo- ptatrienyl radical for one hydrogen atom were obtained.

R = $-CH(COOC_2H_5)_2$, $CH_3COCHCOOC_2H_5$, $O_2NCH-COOC_2H_5$, $N\equiv C-CH-COOCH_3$

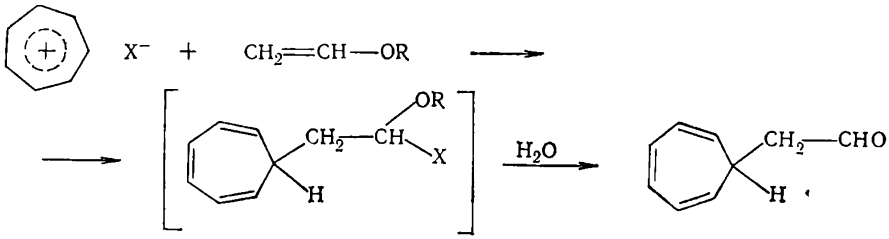
Ketones containing only one carbonyl group without activating bstituents (acetone, acetophenone) can be tropylated under much re drastic conditions. If ketones are heated for a long time with pylium bromide, the α-hydrogen atom is replaced, resulting a mono-substituted product. Introduction of a second carbonyl up activates the molecule substantially. For example, acetyl- tone reacts rapidly with tropylium salts in the cold.

As is known, catalysts are usually required to carry out alkylation reactions (such catalysts may be metal halides which promote the formation of intermediate carbonium ions). Tropylium salts contain a ready-made carbonium ion, and no additional activation is necessary.

"Tropylation" is applicable to aromatics containing strong type I orientants (phenol, hydroquinone, α- and β-naphthols, fluoroglucine) [88].

One of the properties of aliphatic carbonium ions is their ability to attack the double bond of unsaturated compounds to form addition products or polymers.

Tropylium ion is less reactive and therefore it does not react with unsaturated compounds containing an unactivated double bond. However, vinyl ethers react with tropylium salts even in the cold.




The examples given above are reactions of the tropylium cation with nucleophilic reagents resulting in products of addition of the attacking reagent to the tropylium system.

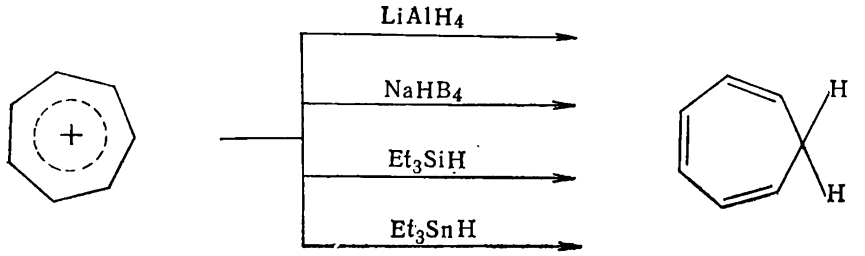
However, nucleophilic substitution in the tropylium nucleus is also known [89, 90]. Thus, tropylium chloride or bromide react readily with water exchanging the halide for the hydroxyl group.

The mechanism of this reaction apparently consists in a nucleophilic attack of the tropylium nucleus by an $H_2O$ molecule or by an $OH^-$ anion accompanied by simultaneous elimination of HBr or $Br^-$.

An interesting reaction takes place when tropylium salts act on cyclopentadienylsodium [89, 90]. A covalent compound 7-cyclopentadienyl-cycloheptatriene-1,3,5 with a dipole moment of 0.6 D results instead of the ionic salt $C_5H_5^- \cdot C_7H_7^+$.

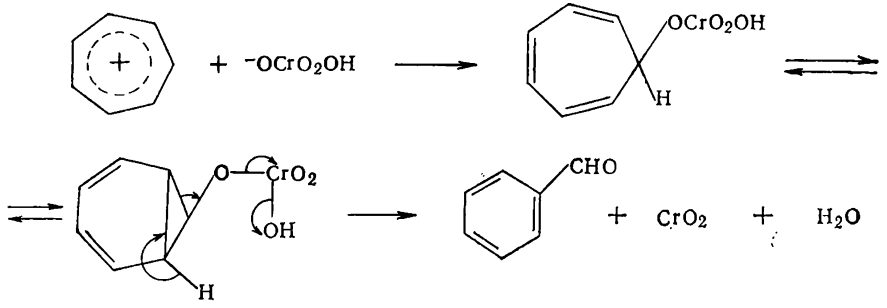
The fact that a covalent bond forms rather than an ionic one will be understood if it is taken into consideration that cyclopentadiene is a very weak acid (its dissociation constant is many orders smaller than $10^{-5}$).

Tropylium can be reduced to cycloheptatriene under the action of such strong hydride-ion donors as lithium aluminium hydride, or sodium borohydride. It is also capable of tearing off hydride ions from triethylsilane and triethylstannane [91]:

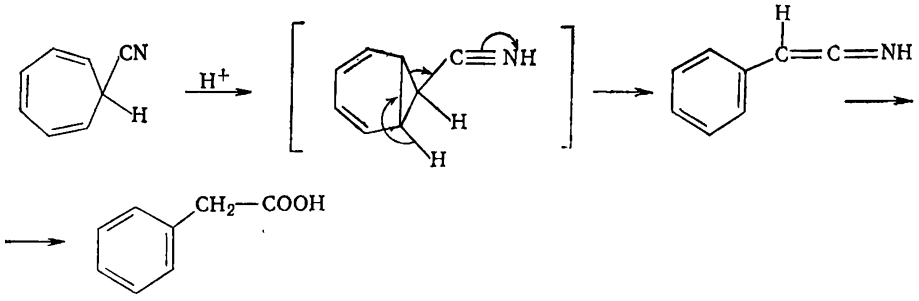



**Rearrangements of Tropylic Systems into Benzenoid Systems**

Tropylium salts can be converted into benzaldehyde by the action of oxidizing agents ($H_2CrO_4$, $Ag_2O$). The following mechanism has been suggested for this reaction [85]:



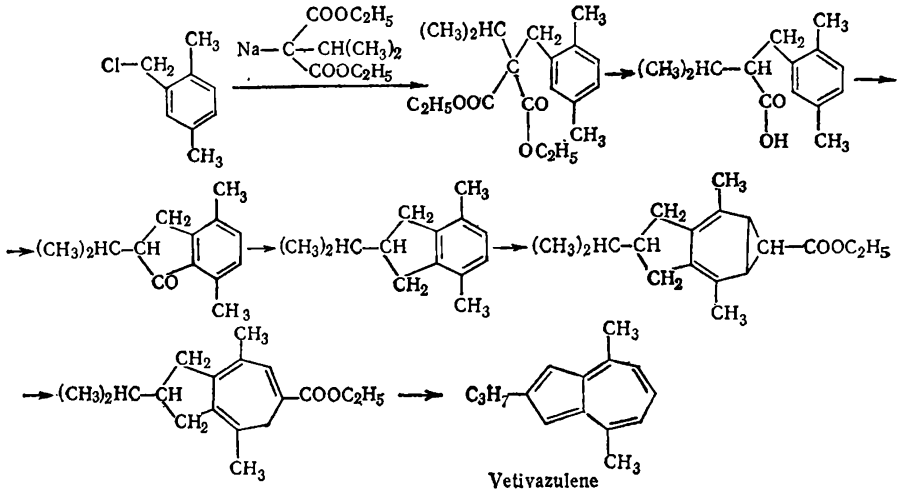

A similar rearrangement takes place in the saponification of tropylium cyanide in acid solution [92]:




Under the action of hydrogen peroxide tropylium salts eliminate one carbon atom and form benzene [93].

### Azulenes

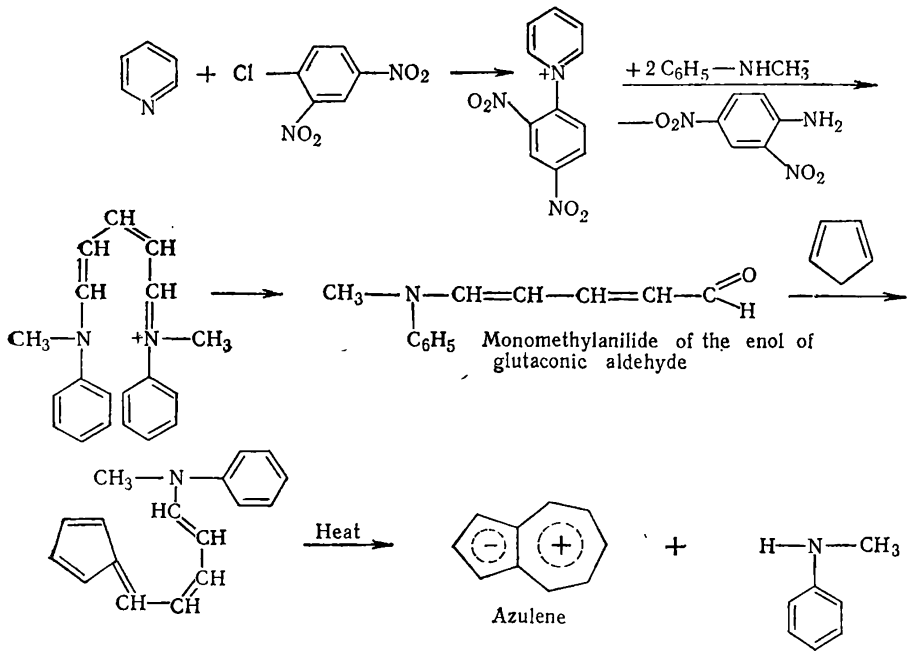
A number of methods of synthesis of azulenes have been worked out. For example, *vetivazulene* can be obtained from 2-chloromethyl-*p*-xylene and sodio-isopropylmalonic ester according to the following scheme:




Ziegler and Hafner [94] worked out a convenient method of preparing azulenes. In this method the addition product of 2,4-dinitrochlorobenzene with pyridine is treated with N-methylaniline to give methylanilide glutaconic aldehyde. The latter is further converted into monomethylanilide of the enol form of glutaconic aldehyde which reacts with cyclopentadiene giving a quantitative yield of the fulvene derivative. This latter compound when heated in vacuo produces azulene in a 60% yield.

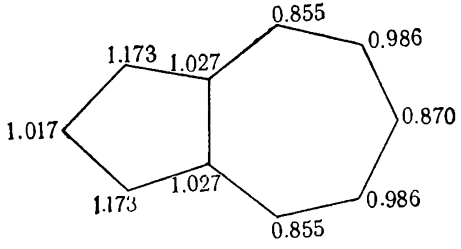
It was shown above (page 472) that the structure of azulene is somewhat better described by formula VI than by formula V, although there is apparently no complete separation of charges, because azulene possesses the properties of an unsaturated compound in many respects. The unsaturated character of azulene is manifested by its dark blue colour. However, partial separation of the charges is responsible for certain aromatic properties of azulene.

Quantum mechanical calculations show that azulene possesses the following $\pi$-electron density distribution ($\pi$-electron density in formula VII greater than unity indicates a negative charge on the atom, smaller than unity—a positive charge).




On the basis of this distribution of π-electron density it was assumed that electrophilic substitution in azulenes should take place in position 1, and nucleophilic or radical substitution, in position 4.

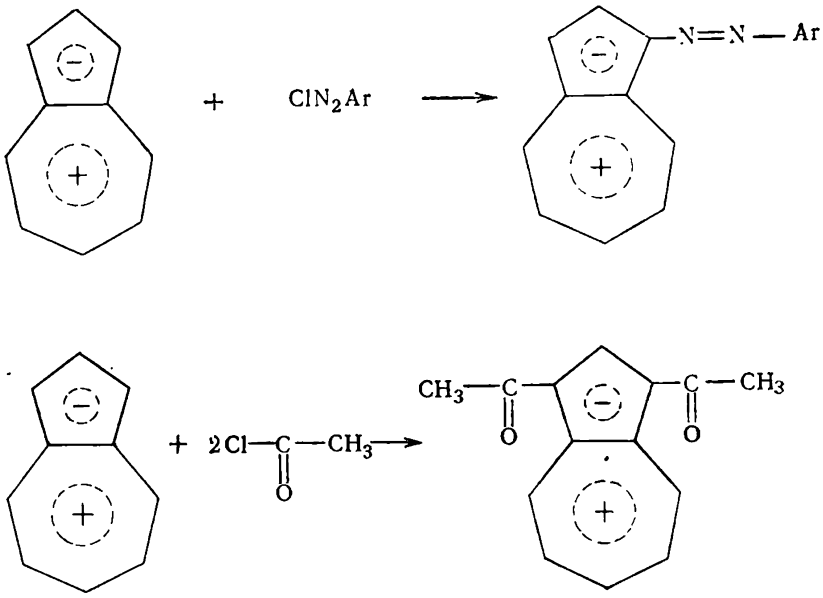
Indeed, the "cyclopentadienyl" nature of azulenes is exhibited in the ease of electrophilic substitution in the five-membered ring. These reactions take place more readily than in naphthalene (isomeric to azulene), the first substituent always entering position 1, the second, position 3.




VII

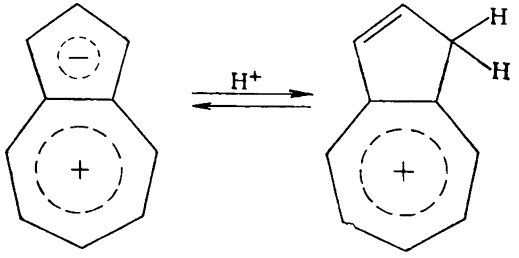
Thus, reactions with diazonium salts result in 1-arylazo substituted azulenes. Friedel-Crafts acetylation of azulene gives the

1,3-diacetyl derivative:




Nitration of azulene under mild conditions (copper nitrate in acetic anhydride) gives 1-nitroazulene and when nitric acid in acetic anhydride is used a mixture of 1-nitro and 1,3-dinitroazulene results. Azulene is easily sulphonated by the dioxane-sulphur trioxide adduct to 1-azulene-1-sulphonic acid.

The properties of azulene as a derivative of the cyclopentadienyl anion are manifested in its ability to be protonated: azulene dissolves in mineral acids forming yellow solutions.

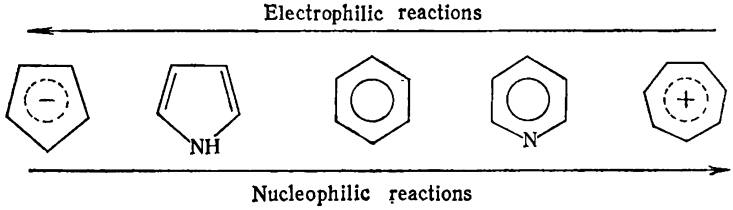



The resulting azulenium cation is actually a substituted tropylium ion and its absorption therefore differs considerably from the absorption (in the ultraviolet) of azulene ($\lambda_{max} = 580$ mμ), being equal to that of benzotropylium ($\lambda_{max} = 352$ mμ). In basicity azulene approaches *o*-nitroaniline ($pK = 0.55$ in formic acid).

Nucleophilic substitution reactions in the seven-membered ring of the azulene molecule have been studied much less than electrophilic substitutions.

It is known that organometallic compounds are capable of addition to azulene [95]. The first radical from the organometallic compound R—Me enters position 4, the second, position 8, that is, the positions of least electron density.

In comparing the reactivity of the aromatic systems considered (5,6,7-member carboxylic and heterocyclic) with regard to electrophilic and nucleophilic reagents it is apparent that they form the following series with regard to increasing reactivity with electrophilic reagents: cyclopentadienyl anion < pyrrole (and analogous five-membered heterocycles) < benzene < pyridine < tropylium. The series of increasing reactivity in reactions with nucleophilic reagents is naturally the reverse.




**Dicyclopentadienyl Organometallic Compounds***

Dicyclopentadienyl iron (ferrocene) and several other dicyclopentadienyl derivatives of transition elements are unusually stable. In spite of the high formal unsaturation, addition reactions are unknown with them. Ferrocene itself participates in a wide range of electrophilic hydrogen substitution reactions, typical of aromatic systems.

A convenient method of synthesizing dicyclopentadienyl organometallic compounds is by treating cyclopentadienylmagnesium bromide with a metal halide (in ether or in a mixture of ether and benzene) e.g.:

$$2C_5H_5MgBr + 2FeCl_3 \longrightarrow 2FeCl_2 + C_5H_5—C_5H_5 + MgBr_2 + MgCl_2$$

$$2C_5H_5MgBr + FeCl_2 \longrightarrow \text{ferrocene} + MgCl_2 + MgBr_2$$

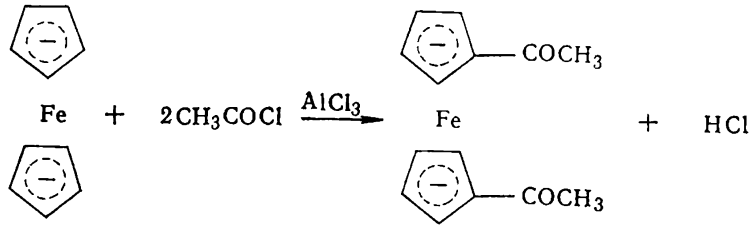
* See [96] for reviews.

Instead of cyclopentadienylmagnesium bromide, cyclopentadienylsodium (or lithium) was used in some cases (Fe, Ti, V, Mo, W, Mn). Sometimes metal acetylacetonates are used in lieu of the halides (Ni, Co, Ru, Rh, Ir).

The electronic structure of dicyclopentadienyl derivatives is of great interest from the point of view of understanding the causes responsible for their aromatic properties [97]. For the electronic structure of ferrocene see Chapter 1.

Ferrocene is remarkably stable for an organometallic compound and is capable of substitution reactions characteristic of aromatic systems.

Thus, it is capable of acylation, alkylation, sulphonation, diazotizing arylation, etc.



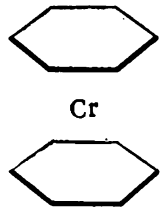

$$(C_5H_5)_2Fe \xrightarrow{SO_3 \cdot \text{dioxan}} C_5H_5FeC_5H_4SO_3H \cdot 2H_2O$$

$$(C_5H_5)_2Fe \xrightarrow{ArN_2X} C_5H_5FeC_5H_4Ar + N_2 + HX$$

Attempts to carry out similar reactions of electrophilic substitution for dicyclopentadienyl compounds of other metals (in particular for Ni, Co, Ti) were unsuccessful.

#### Dibenzenechromium

Dibenzenechromium possesses a centrosymmetrical sandwich structure with parallel benzene rings and the chromium atom between them in the centre of symmetry.



The dibenzenechromium ion can be synthesized with the aid of he so-called Friedel-Crafts reductive method [98],

$$3CrCl_3 + 2Al + AlCl_3 + 6C_6H_6 \longrightarrow 3[Cr(C_6H_6)_2]^+AlCl_4^-$$

The cation can be precipitated as the iodide, perchlorate, picate and others. Reduction of the $[Cr(C_6H_6)_2]^+$ cation results in lectrically neutral dibenzenechromium:

$$2[Cr(C_6H_6)_2]^+ + S_2O_4^{=} + 4OH^- \longrightarrow 2Cr(C_6H_6)_2 + 2SO_3^{=} + 2H_2O$$

Dibenzenechromium is brownish black, moderately soluble in rganic solvents, insoluble in water, thermally stable up to 300°, nd is easily oxidized to the cation.

The benzene rings of dibenzenechromium are devoid of the reactiity characteristic of aromatic compounds. Neither electrophilic, or radical, nor nucleophilic substitution reactions take place with ibenzenechromium.

Similar properties are exhibited by dibenzenemolybdenum and ibenzenevanadium.

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# 9

# MOLECULAR REARRANGEMENTS

In the majority of cases only portions of the reacting molecules participate and undergo changes in organic reactions. As a result of this, groups of atoms are transferred unchanged from one molecule to another just like atoms of elements go from one molecule to another.

This phenomenon, observed at the time when the radical theory was still dominant, has been and is of great significance in establishing a structure by chemical means. At present, however, a considerable number of reactions are known where structural changes occur in parts of the molecules not directly participating in the reaction.

Such reactions are known as *molecular rearrangements.*

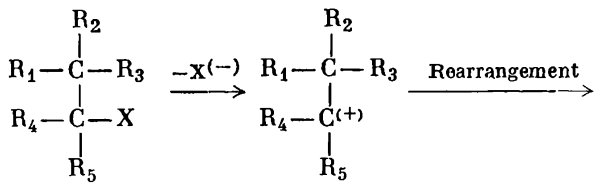
## 9-1 REARRANGEMENTS IN THE ALIPHATIC SERIES

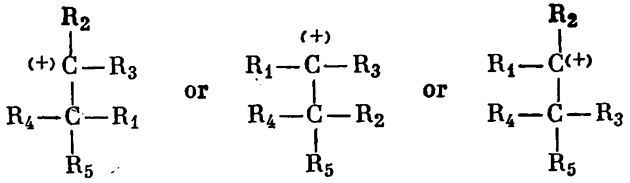
### 9-1.1 Nucleophilic Rearrangements in the Aliphatic Series

Nucleophilic (or anionotropic) rearrangements are rearrangements in which a group carrying an excess of electrons migrates to a centre where there is a deficiency of electrons.

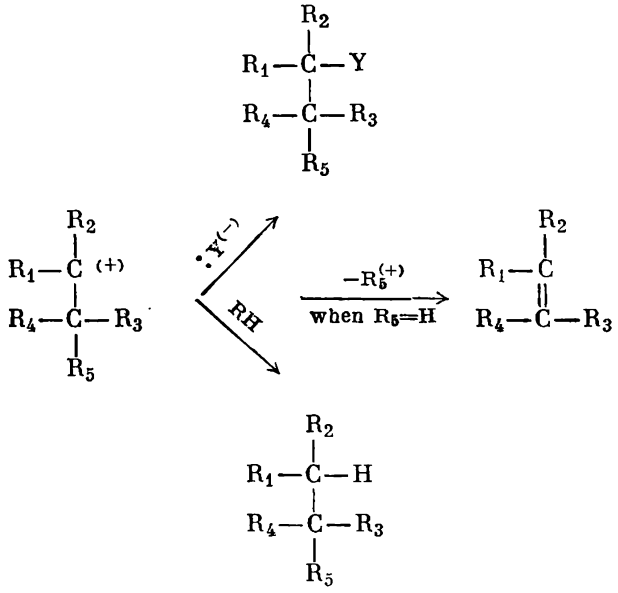
This section will deal with nucleophilic rearrangements in the aliphatic series, including not only rearrangements in saturated systems, but also nucleophilic rearrangements of unsaturated and aromatic compounds, in which the multiple bonds do not play a determining part.

Nucleophilic aliphatic rearrangements proceed according to the following general scheme:

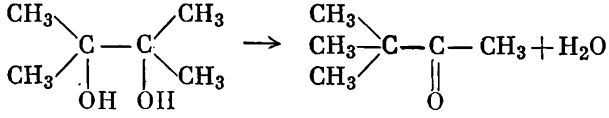




The carbonium ion formed reacts further, e.g.:



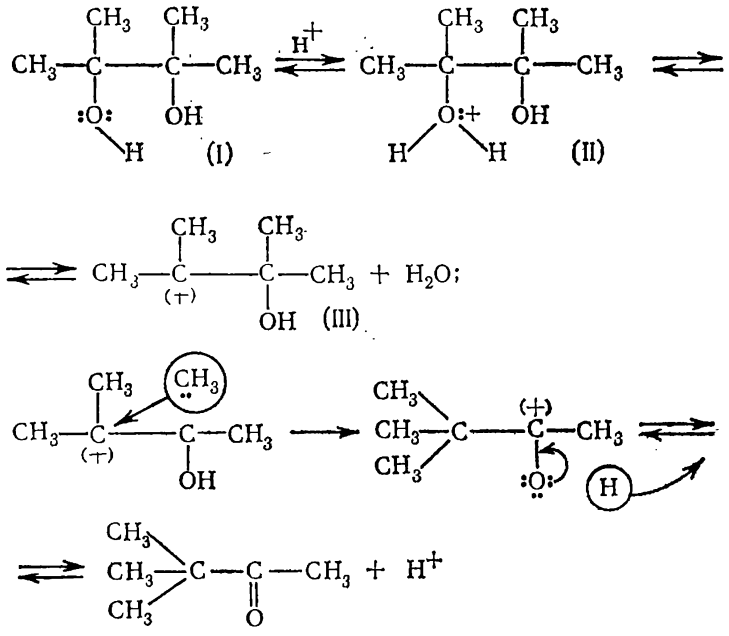
**Pinacol-Pinacolone Rearrangement** [1]. When ditertiary alcohols—*pinacols*—are acted on by mineral acids, acid chlorides, zinc chloride and other electrophilic agents, water is eliminated, resulting in the formation of ketones—*pinacolones.*



This reaction, discovered by Butlerov [2], is called *pinacol-pinacolone rearrangement.*

In accordance with the general scheme for nucleophilic rearrangements of saturated systems, the mechanism of pinacol-pinacolone

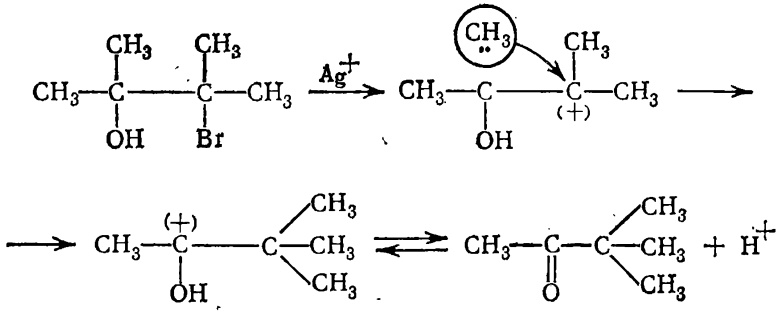
rearrangement may be represented as follows:



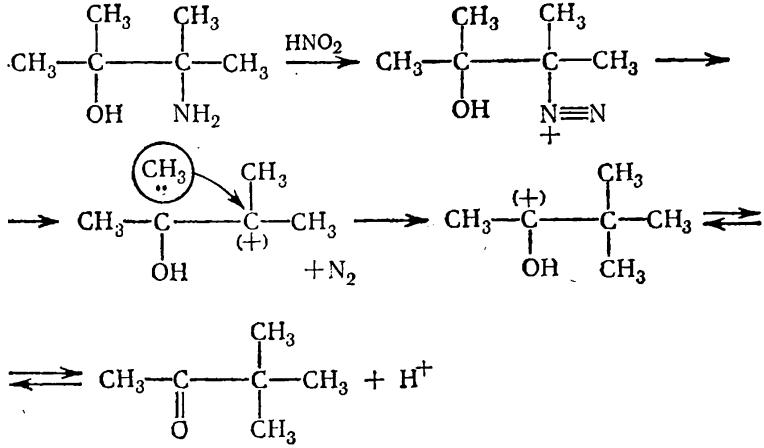
(IV)

It is obvious that according to this scheme the determining step of reaction is the formation of the intermediate carbonium ion (III).

If the scheme is correct, then other reactions in which the formation of such a carbonium ion is possible may also result in the formation of a pinacolone. That this is actually so has been confirmed experimentally. For example, pinacolone forms in the reaction between silver oxide or silver nitrate and pinacol bromohydrin [3]:

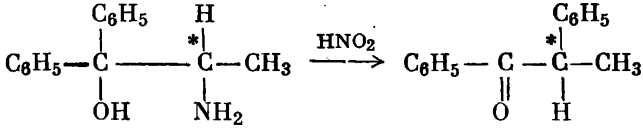


2,3-Dimethyl-3-aminobutanol-2 undergoes the same transformation when treated with nitrous acid [4]:

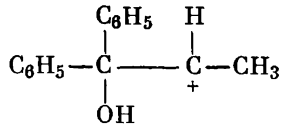


The above schemes represent pinacol-pinacolone rearrangement as an aggregate of discrete stages. Actually, it is apparently a continuous process.

This is confirmed, for example, by the results of a study of the stereochemistry of the following pinacol-pinacolone rearrangement.

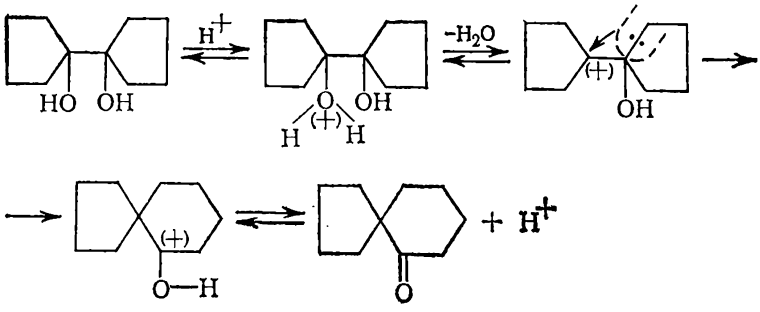


The above reaction proceeds with a Walden inversion at the asymmetric carbon atom [5]. If the carbonium ion

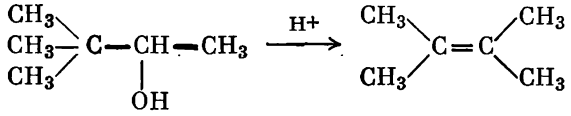


formed as a kinetically independent particle one should have expected a racemic mixture to result.

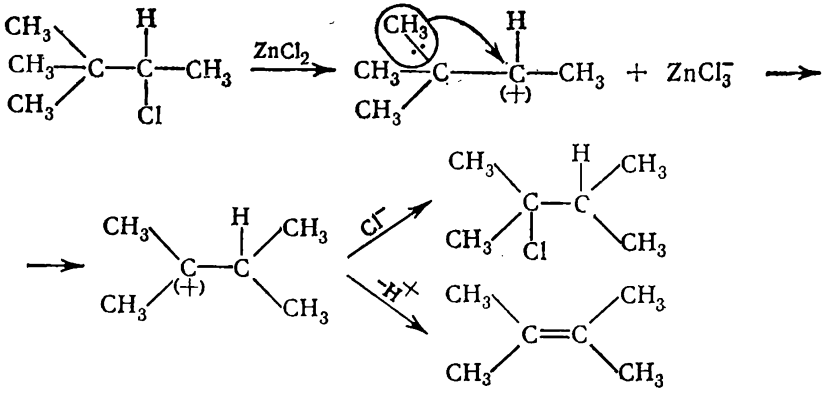
A singular example of pinacol-pinacolone rearrangement is the transformation of cyclic pinacols into ketones of the spiran series [6]:



**Retropinacol-Pinacolone Rearrangement.** When 2,2-dimethyl-3-hydroxybutane (pinacolic alcohol) is heated with anhydrous oxalic acid, one of the reaction products is tetramethylethylene [7]:

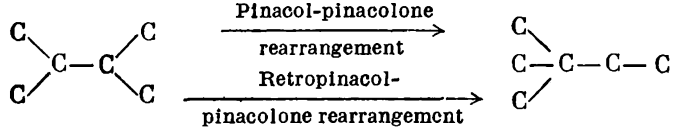


This reaction is an example of retropinacol-pinacolone rearrangement proceeding according to a mechanism quite analogous to that of pinacol-pinacolone rearrangement. The corresponding halogen derivatives also undergo retropinacol-pinacolone rearrangement under the influence of zinc chloride, e.g.:



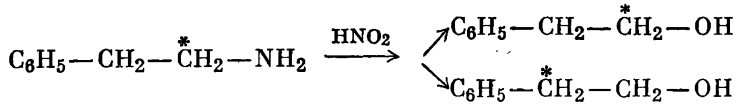
The formation of alkenes is the predominant reaction in the rearrangement of alcohols.

As we see, the change in the carbon skeleton of the reacting molecules in the pinacol-pinacolone rearrangement is directly opposite* to that in the retropinacol-pinacolone rearrangement.

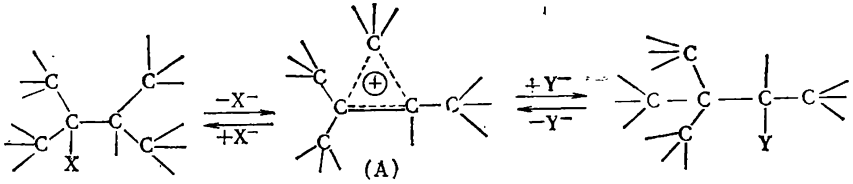



These rearrangements are two sides of the same reversible process, the predominant direction of which depends on the reaction conditions. That is why the mechanism of the rearrangements is the same.

* There are, however, rearrangements of this type where the change in the carbon skeleton can be established only by using a labeled carbon, e.g.:

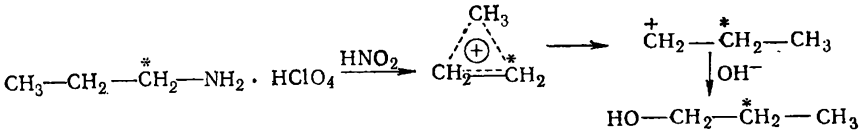


In particular, both rearrangements take place via the same nonclassical cation (A):



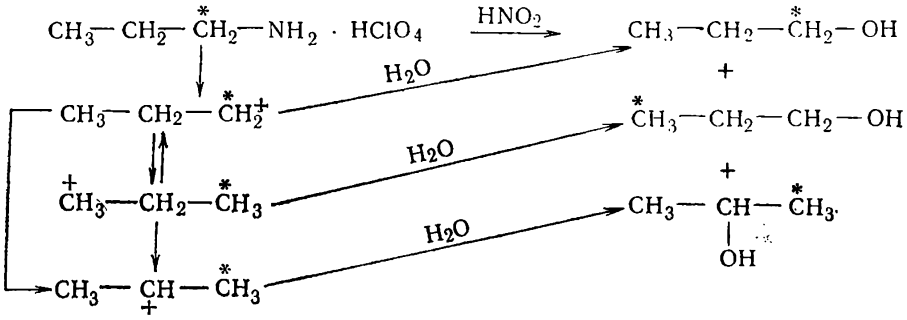
## 9-1.2 Synartetic Acceleration

It was thought that the simplest pinacol-pinacolone rearrangement proceeding through the stage of formation of the simplest nonclassical cation is that which occurs in the reaction between *n*-propylamine perchlorate and nitrous acid.



This conclusion was made on the basis of an investigation of the reaction with *n*-propylamine having $C^{14}$ in position 1 [8].

However, it was discovered recently [9] that no skeletal rearrangement is involved in this reaction. In reality, isomerization of the propyl cation occurs through transfer of a hydride ion from the β-position (as well as from the α-position).

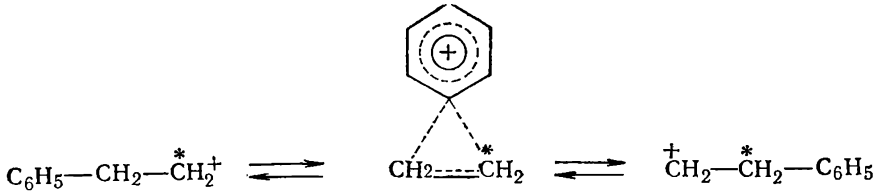


It is interesting that skeletal isomerization of the pinacol-pinacolone rearrangement type takes place if a methyl group in the propylamine molecule is exchanged for an aromatic radical, say, for phenyl.

β-Phenylethylamine labeled with $C^{14}$ at the β-carbon atom gives a mixture of two alcohols when treated with nitrous acid [10].

$$C_6H_5-CH_2-\overset{*}{C}H_2-NH_2\cdot HClO_4 \xrightarrow{HNO_2}$$
$$\longrightarrow C_6H_5-CH_2-\overset{*}{C}H_2-OH + C_6H_5-\overset{*}{C}H_2-CH_2-OH$$

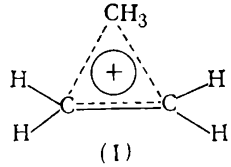
The mechanism of formation of the second alcohol may be explained by assuming that a non-classical cation (B) forms as an intermediate.



(B)

This non-classical cation should be very stable because of delocalization of its positive charge by the benzene ring.

It is conceivable that in the case of the *n*-propyl cation, hydride transfer from the β-position takes place in preference to skeletal isomerization because the latter would result in the least stable (simplest) non-classical cation (I) with the least delocalized positive charge[1].



(I)

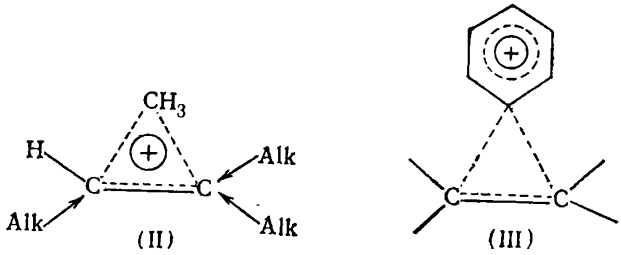
In more complex cases, when one or several hydrogens are exchanged for alkyl groups, the latter partly neutralize the charge by induction and stabilize the non-classical cation (II). It should be expected that the stability of cations of this type (III) will be the highest when the π electrons of aromatic nuclei participate in the delocalization of the positive charge.

A large number of rearrangements are known where the formation of intermediate non-classical cations of type (III) (phenonium

---

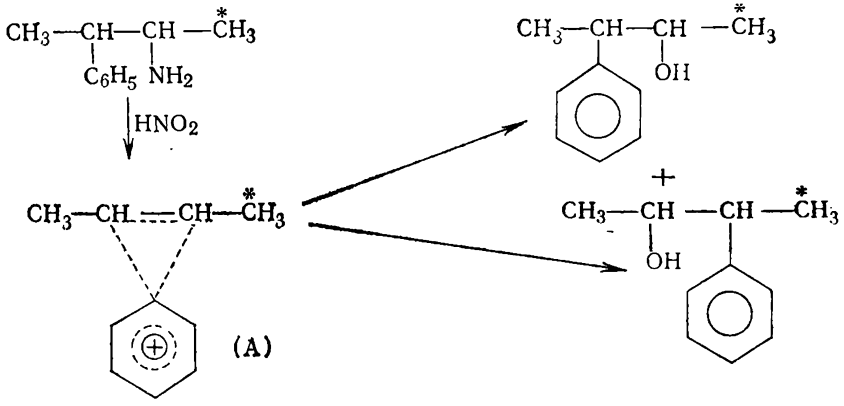
[1] Such a non-classical cation is formed apparently on isomerization of propane-1-$C^{13}$ into propane-2-$C^{13}$ under the influence of $AlBr_3$ [43].

cations) must be assumed.



(II) (III)

For instance, the reaction of 2-amino-3-phenylbutane-1-$C^{14}$ with nitrous acid results in 3-phenylbutanol-2, with the $C^{14}$ in positions 1 and 4 in a 1 : 1 ratio [11]:



This is readily explained by the formation of the intermediate phenonium ion (A).

It is to be expected that electron-donor substituents in the benzene ring which favour additional delocalization of the positive charge should facilitate rearrangement. Conversely, electronegative substituents should impede rearrangement.

Investigation of the rearrangement in the reaction of aryl amines with nitrous acid confirms these assumptions [12, 13]

$$p\text{-}XC_6H_4-CH_2-\overset{*}{C}H_2-NH_2 \xrightarrow{HNO_2} p\text{-}XC_6H_4-\overset{*}{C}H_2-CH_2-OH$$

(when $X = CH_3O$, the rearrangement proceeds to an extent of 33-45 %[1]; when $X = H$, $\sim$ 22 %; when $X = NO_2$, $\sim$ 5 %).

It should be noted that such neighbouring groups as phenyl accelerate not only rearrangements but substitution processes as well (those involving rearrangements, as well as those proceeding without rearrangements).

[1] Depending on the solvent (water or acetic acid).

Thus, of the two esters I and II of *p*-bromobenzenesulphonic acid

$$(CH_3)_2\overset{C_6H_5}{\overset{|}{C}}-CH_2-O-SO_2-C_6H_4-Br \quad (I)$$

$$(CH_3)_2\overset{CH_3}{\overset{|}{C}}-CH_2-O-SO_2-C_6H_4-Br \quad (II)$$

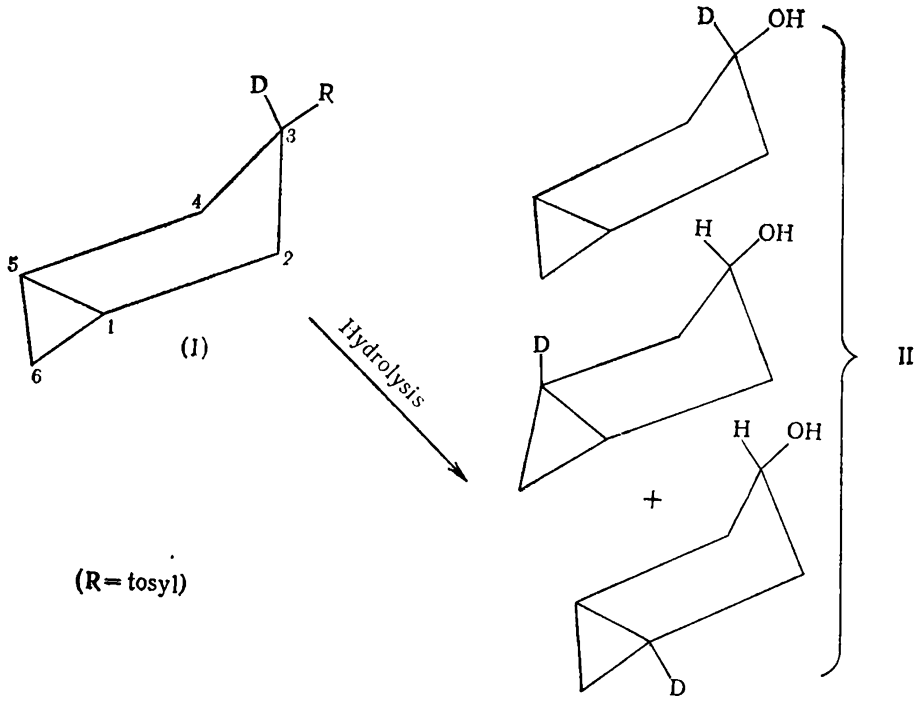
the first, which contains a phenyl group, acetolyzes 250 times faster than the second [13].

Acceleration of substitution or rearrangement under the influence of neighbouring groups is called *synartetic acceleration**.

The causes of synartetic acceleration in rearrangements and substitution reactions have been discussed by many authors [14-17].

Currently the accelerating action of the phenyl and other such groups is explained by delocalization of the positive charge of the intermediate carbonium ion by the $\pi$ electrons of the benzene ring.

If such a non-classical cation forms during a solvolysis reaction, not involving a rearrangement, the acceleration of this reaction is also due to the formation of the non-classical cation.

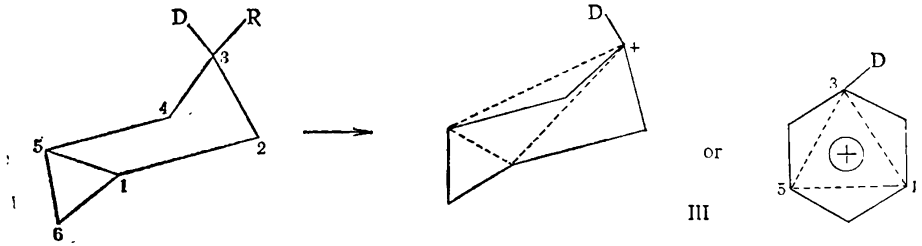



* *Anchimeric facilitation* is a less widely used expression.

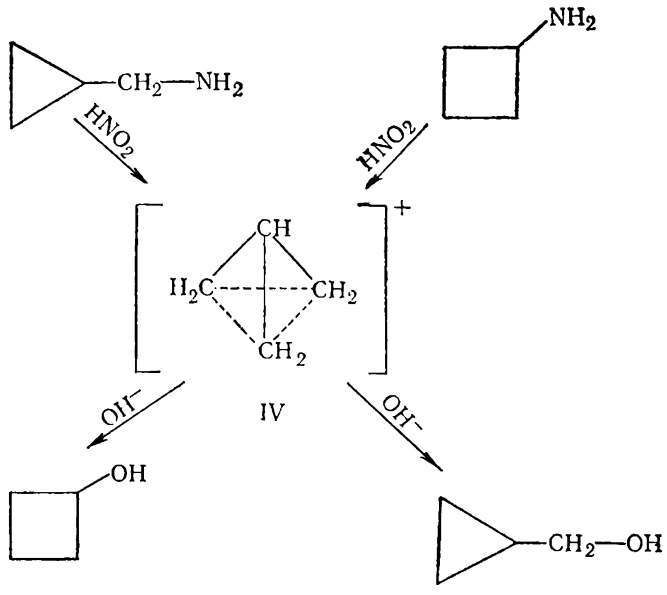
Recently a number of reactions of aliphatic compounds have been discovered during which non-classical carbonium ions are formed with charges equally distributed among similar carbon atoms.

A vivid illustration is the hydrolysis of tosylate I, containing a deuterium atom in position 3 investigated by Winstein [18]. The reaction results in the formation of an alcohol (II) with deuterium evenly distributed among positions 1,3 and 5, of its molecules.

This is explained as follows. In the intermediate carbonium ion the positive charge is not localized in position 3. Bonds form between $C_3$, $C_1$ and $C_5$ ($C_1$ — $C_3$ and $C_3$ — $C_5$) and at the same time the $C_1$ — — $C_5$ bond is weakened. The non-classical cation contains the equivalent bonds $C_1$ — $C_3$, $C_3$ — $C_5$ and $C_5$ — $C_1$. Therefore, the probability of addition of an OH anion at atoms $C_1$, $C_3$ or $C_5$ is the same.




Roberts and coworkers [19] confirmed the formation of non-classical carbonium ion IV in a study of the distribution of $C^{14}$



in cyclopropylcarbinol and cyclobutanol formed by the action of nitrous acid on cyclopropylamine-2-$C^{14}$ (or on cyclobutylamine-2-$C^{14}$).

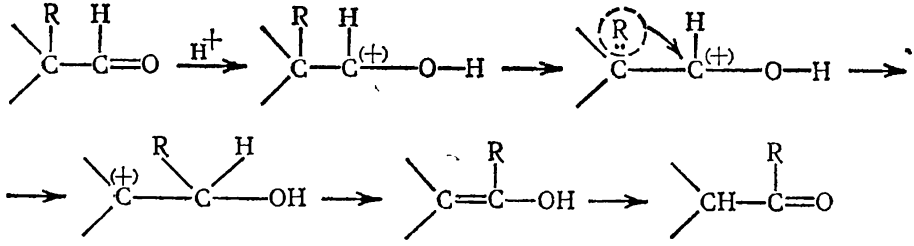
It was shown that in the course of the reaction the three methylene groups are equivalent.

**Aldehyde-Ketone Rearrangement.** The transformation of aldehydes into isomeric ketones is accompanied by exchange of the aldehyde hydrogen for the neighbouring hydrocarbon group. It takes place under the action of concentrated sulphuric acid, e.g. [20]:

$$(CH_3)_3C{-}CHO \xrightarrow{H_2SO_4} (CH_3)_2CH{-}\overset{\overset{O}{\|}}{C}{-}CH_3$$

$$(C_6H_5)_2CH{-}CHO \xrightarrow{H_2SO_4} C_6H_5{-}CH_2{-}\overset{\overset{O}{\|}}{C}{-}C_6H_5$$

The mechanism of transformation of aldehydes into ketones is apparently similar to that of retropinacol-pinacolone rearrangement and may be represented by the following diagram:



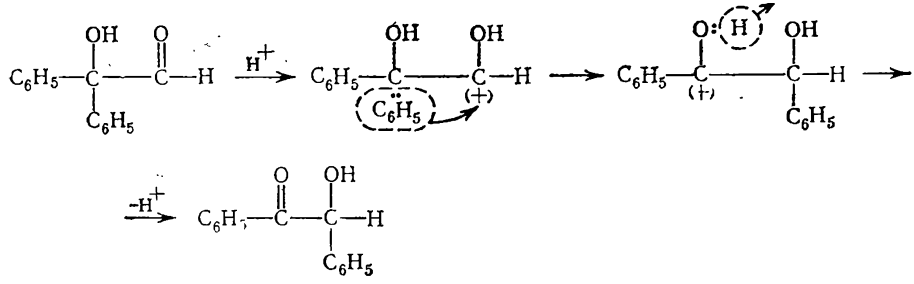
**Acyloin and Benzilic Acid Rearrangements.** The transformation of α-hydroxyaldehydes or α-hydroxyketones into isomeric α-hydroxyketones under the influence of an alcoholic solution of sulphuric acid is called acyloin rearrangement:

$$C_6H_5{-}\overset{\overset{C_6H_5}{|}}{\underset{OH}{C}}{-}\overset{\overset{O}{\|}}{C}{-}H \rightarrow C_6H_5{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{C_6H_5}{|}}{\underset{OH}{C}}{-}H \quad [21]$$

or

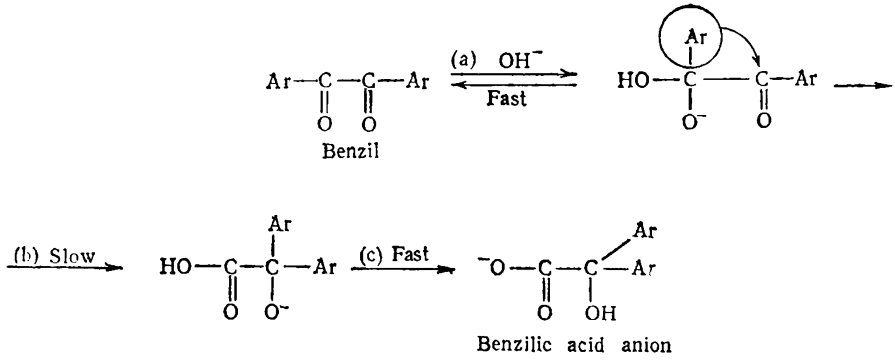
$$CH_3{-}\overset{\overset{CH_3}{|}}{\underset{OH}{C}}{-}\overset{\overset{CH_3}{|}}{\underset{O}{C}}{-}CH \rightarrow CH_3{-}\overset{\overset{CH_3}{|}}{\underset{O}{C}}{-}\overset{\overset{CH_3}{|}}{\underset{OH}{C}}{-}CH \quad [22]$$

Acyloin rearrangement probably proceeds according to the mechanism of retropinacol-pinacolone rearrangement, e.g.:



The transformation of benzil into benzilic acid under the action of an alkali was discovered by Liebig [23]. It is called *benzilic acid rearrangement.*

The intermediate product of the addition of potassium hydroxide to benzil, $C_6H_5COCOC_6H_6 \cdot KOH$ has been isolated. It has also been shown that it is capable of rearrangement into potassium benzilate, $(C_6H_5)_2C(OH)COOK$. The rate of benzilic acid rearrangement is proportional to the concentration product [benzil] $[OH^-]$. All these facts are in agreement with the mechanism of benzilic acid rearrangement given above [24]:



That step (*a*) is fast and reversible follows from the results of a study of the rearrangement in $H_2O^{18}$. The diketone suffers $O^{18}$-exchange in $H_2O^{18}$ in the presence of a base at a rate considerably faster than that of the rearrangement [25].

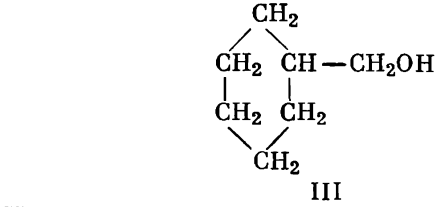
It should be noted that the mechanism of simultaneous transfer of aryl and proton proposed by some workers is incorrect, because the rate of rearrangement in $D_2O$-dioxane is almost twice that of in $H_2O$-dioxane. If hydrogen transfer occurred during the slow stage, determining the overall rate of the rearrangement, the rate ratio would have been the reverse [26].

As is shown in the diagram, benzilic acid rearrangement is similar to acyloin rearrangement, but proceeds according to the pinacol-pinacolone type rather than according to the retropinacol-pinacolone type.

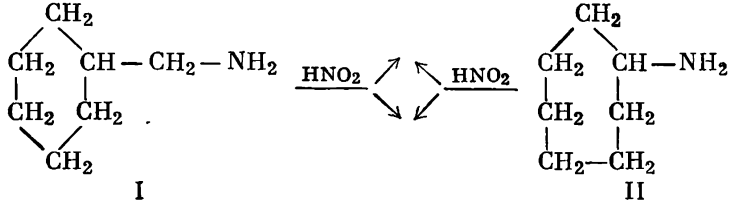
**Dem'yanov Rearrangement.** The most thoroughly investigated of the reactions of expanding and contracting rings is the Dem'yanov rearrangement [27], which takes place when nitrous acid reacts with alicyclic amines.

For example, when cyclohexylmethylamine (I) is treated with nitrous acid, a mixture of cyclohexylcarbinol (III) and cycloheptanol (IV) is formed.

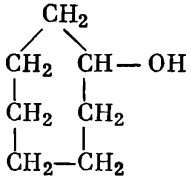
The same mixture of alcohols is formed when nitrous acid reacts with cycloheptylamine (II).



III



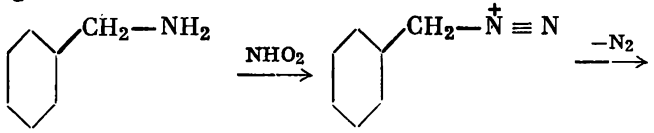

I II



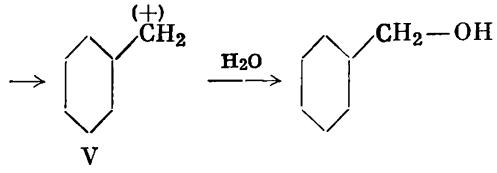
IV

The mechanism of the Dem'yanov rearrangement is similar to the mechanisms of pinacol-pinacolone and the retropinacol-pinacolone rearrangements.

Thus, the formation of cyclohexylcarbinol when nitrous acid acts on cyclohexylmethylamine (I) may be explained by the following diagram:

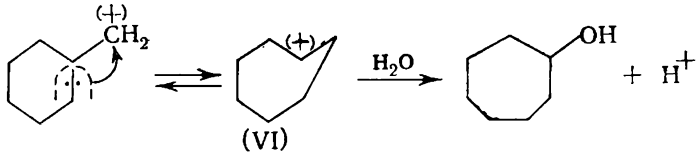



I



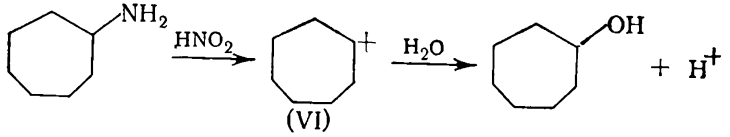

V

However, the carbonium ion (V) may suffer a rearrangement of the retropinacol-pinacolone type giving rise to the carbonium ion (VI) and cycloheptanol.



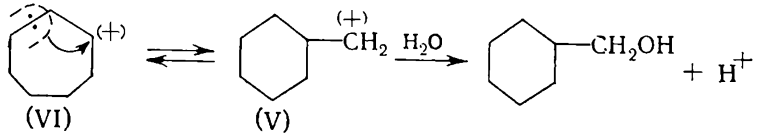

(VI)

The reaction between nitrous acid and cycloheptylamine results in carbonium ion (VI) which reacts with water to yield cycloheptanol:




(VI)

and then undergoes a rearrangement of the pinacol-pinacolone type to form carbonium ion (V) followed by the formation of cyclohexylcarbinol.



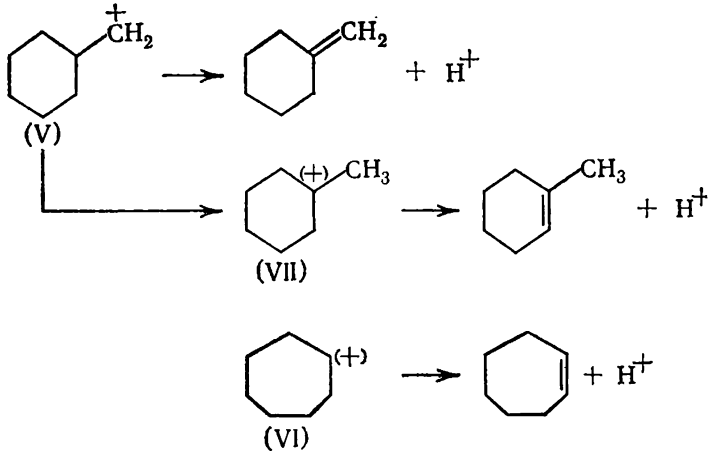

(VI) (V)

Thus, whether nitrous acid reacts with cyclohexylmethylamine or cycloheptylamine, an equilibrium is reached in the reaction mixture between the carbonium ions (V) and (VI), resulting in the same mixture in both cases.

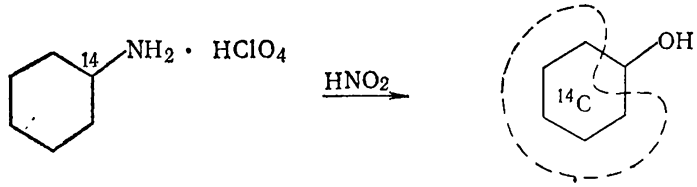
Like the pinacol-pinacolone and retropinacol-pinacolone rearrangements, the Dem'yanov rearrangement may be accompanied by alkene formation owing to the elimination of a proton from the carbonium ions (V), (VI) or (VII).

Besides the elimination of protons from carbonium ions the Dem'yanov reaction is complicated further by hydride transfers, as has been proved in the case of the reaction between cyclohexylamine

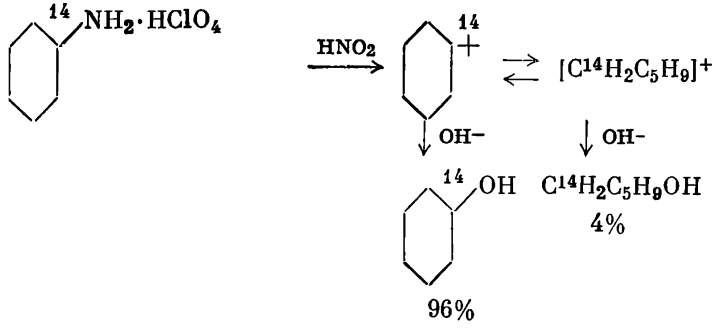
perchlorate labeled with $C^{14}$ in position 1 and nitrous acid. Besides the expected cyclohexanol, another cyclohexanol was found in




which the hydroxyl was linked with a non-radioactive carbon atom and $C^{14}$ was present in the methylene groups of the ring [28]:




It follows from this that the cyclohexyl cation intermediate suffers isomerization due to migration of hydride anions*:

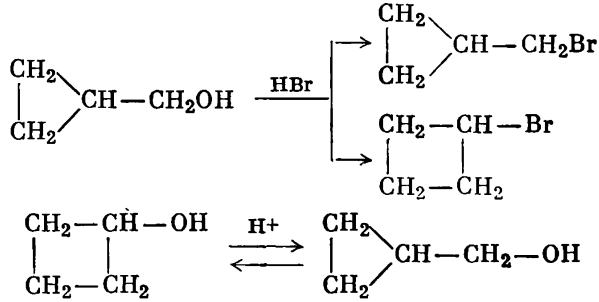



* It has been proved that isomerization takes place during deamination of cyclohexylamine, as well as during solvolysis of cyclohexyl tosylate, essentially because of 1-3 hydrogen shifts.

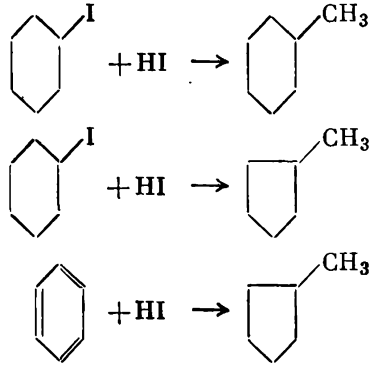
The small amount of isomerization is due to the short life span of the cyclohexyl cation. This hypothesis has been confirmed by the work of Streitwieser and Coverdall [29], who obtained not less than 94% cyclohexanol-2-D from *cis*-cyclohexylamine-2-D perchlorate. If the cyclohexyl cation existed under the conditions of the reaction for a longer time the retention of configuration could not have been so high.

Ring contraction and expansion is observed not only in the reaction of amines with nitrous acid but in other cases as well, where corresponding carbonium ions are formed.

Dem'yanov and Kizhner, for example, established that the reaction of hydrobromic acid with cyclopropylcarbinol results in cyclopropylmethyl bromide and cyclobutyl bromide, while cyclobutanol forms cyclopropylcarbinol under the action of an acid [31]:




Reduction of cycloalkyl iodides [32] and benzene [33] with hydroiodic acid at 250-270° also involves isomerization of the rings.

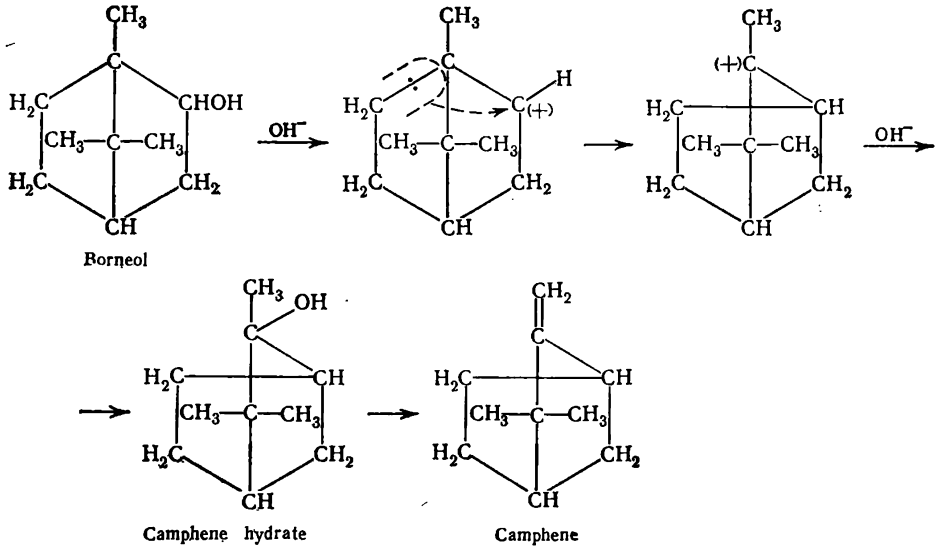



However, the latter reactions, contrary to those cited earlier, are apparently homolytic and proceed through stages of neutral radical formation rather than of carbonium ions.

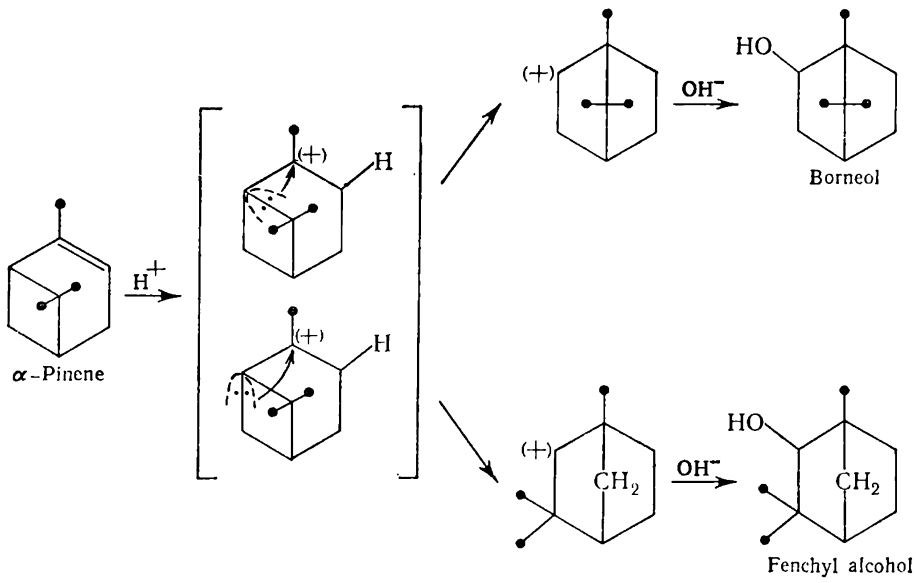
**Wagner Rearrangement.** As it was pointed out earlier (page 553) dehydration of pinacol results in a retropinacol-pinacolone rearrangement.

Such a rearrangement occurs also in the terpene series where it is called the Wagner or Wagner-Meerwein rearrangement.

This rearrangement was discovered by Wagner during a study of the conversion of borneol into camphene [34]:

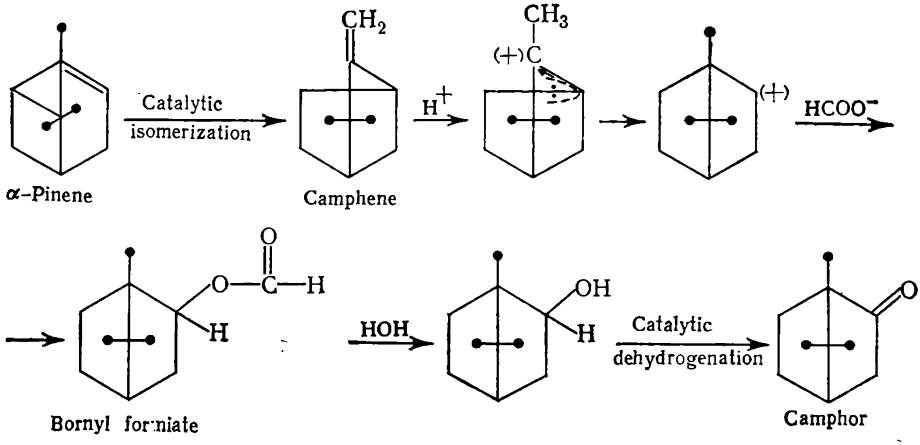



Another example of the Wagner rearrangement is the conversion of α-pinene into borneol and fenchyl alcohol [35]:



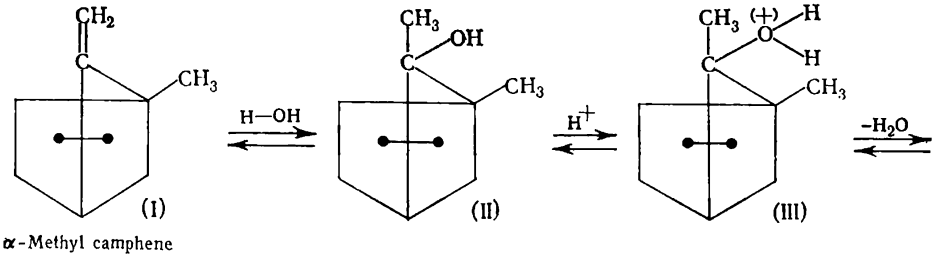
Meerwein carried out a number of important investigations of the Wagner rearrangement [36].

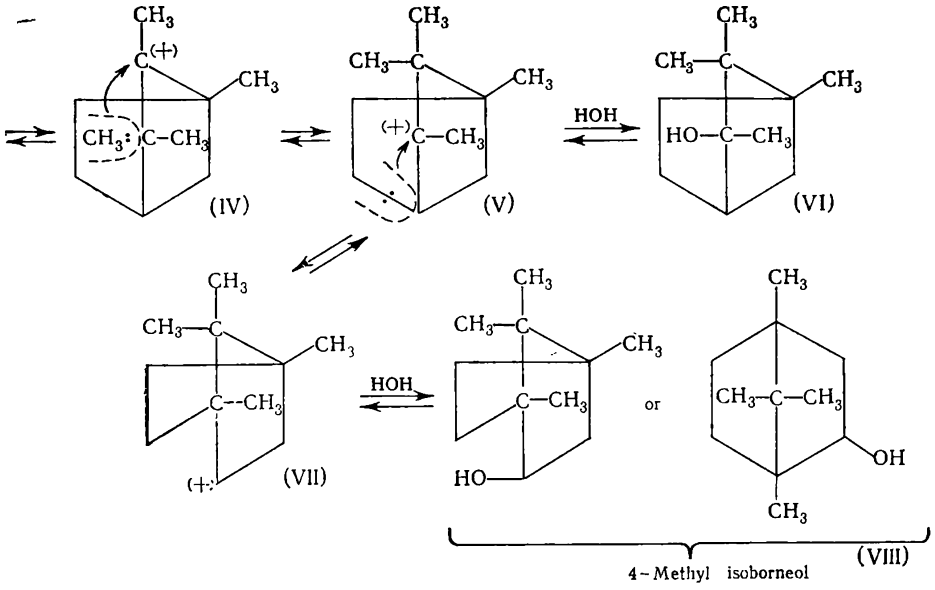
Numerous isomerizations in the terpene series follow the Wagner rearrangement mechanism. Besides, the commercial synthesis of camphor from α-pinene after Tishchenko also proceeds through a Wagner rearrangement:




In this synthesis the addition of formic acid to camphene resulting in the formation of bornyl formiate is accompanied by a Wagner rearrangement.

**Namyotkin Rearrangement** [37]. In investigating the interconversions of α-methylcamphene and 4-methylisoborneol, Namyotkin found that these interconversions result from a more complex rearrangement than Wagner's. This rearrangement is called camphene rearrangement, rearrangement of the second type and recently generally the Namyotkin rearrangement:






Application of the Namyotkin rearrangement mechanism makes it easy to understand the process of racemization in the transformation of isoborneol to camphene on the one hand, and the reasons why racemization is impossible in the transformation of 4-methyl isoborneol to α- and β-methyl camphene, on the other.

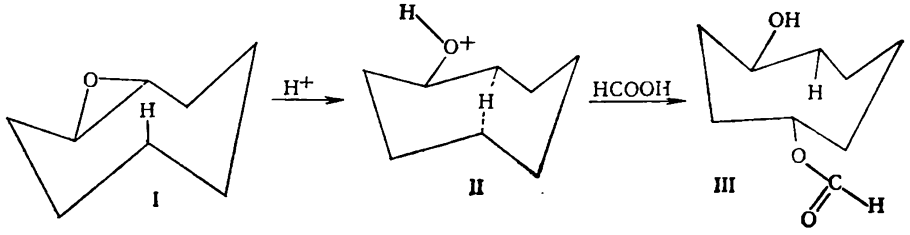
The mechanism of Namyotkin's rearrangement, though more complicated than that of the Wagner rearrangement, is similar to the latter and consists in isomerization of the carbon skeleton according to the retropinacol-pinacolone (or, in the reverse process, the pinacol-pinacolone) rearrangement.

**Transannular Rearrangement.** Rearrangements in which the point of the severance of the group at the beginning and the location of its final addition are separated by one, two or more atoms are quite rare. There are, however, certain cyclic systems in definite conformations, wherein spatial approach of chemically unbound atoms and groups is possible, which are exceptions.

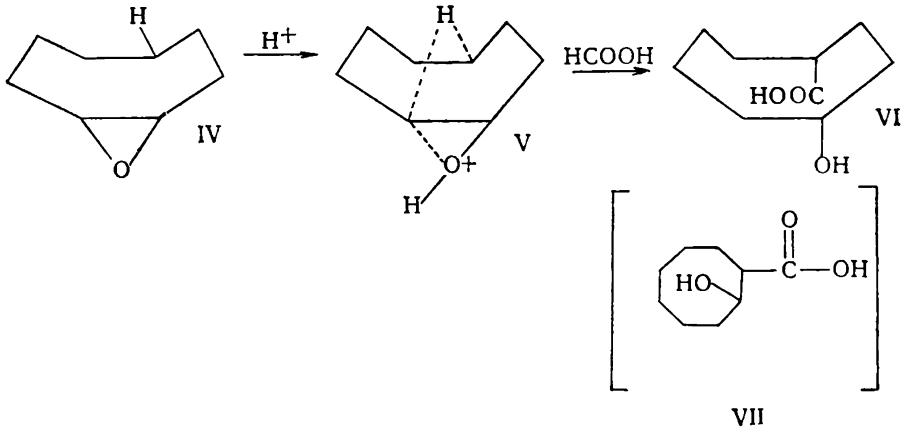
In such cases *transannular rearrangements* are possible.

The rearrangement of a cyclooctyl system given below, involving 1,3-hydride shift, may serve as an example of a transannular rearrangement [38]. It was found that formolysis of epoxy *trans*-cyclooctene (I) yields predominantly *trans*-1,4-monoformiate (III). This result may be attributed to the formation of an intermediate bridge

cation (II):




Similarly, formolysis of epoxy *cis*-cyclooctene (IV) yields appreciable quantities of *cis*-1,4-monoformiate (VI), besides the expected product (VII).




The fact that both reactions are stereospecific indicates that classical intermediate carbonium ions do not form.

An analogous mechanism may be proposed for the conversion of *trans*-cyclooctene dibromide into *trans*-1,4-diacetoxycyclooctene under the influence of silver acetate and acetic acid [39].

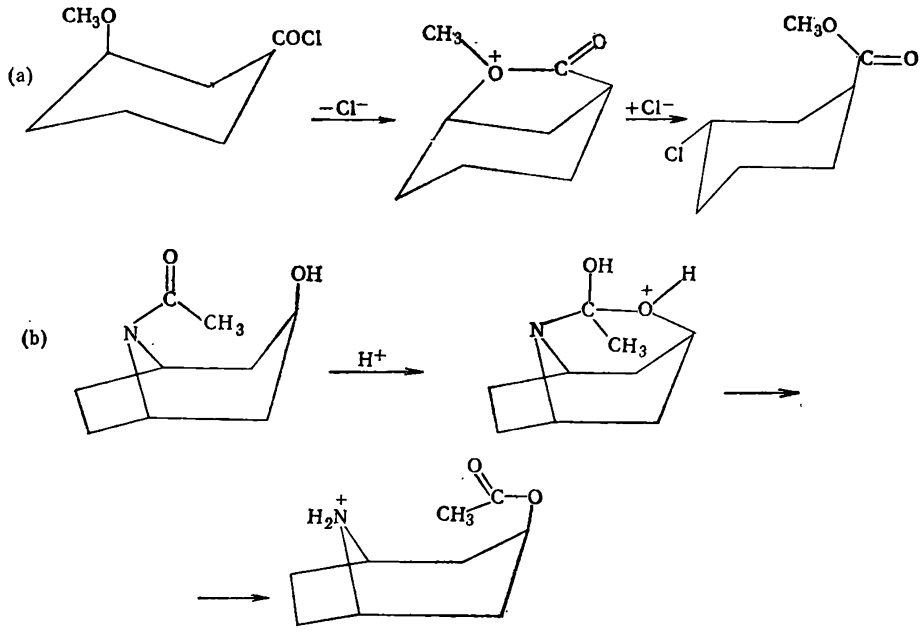
The transannular effect of hydrogens is observed in the solvolysis of cyclooctyl, cyclononyl and cyclodecyl tosylates, because these compounds acetolyze 20-30 times faster than cyclopentyl tosylate and 300-500 times faster than cyclohexyl tosylate.

Using a labeled carbon Fodor [40] proved the transannular migration of hydrogen during the solvolysis of a cyclodecyl compound.

Transannular rearrangements are not limited to the shift of hydrogens only.

Given below are two transannular rearrangements (a) and (b). In the first of them (nucleophilic) the migrating group is a methoxy

group [41], in the second (electrophilic) it is an acetyl [40].



**Isomerization of Alkanes.** Under the action of acid catalysts, such as sulphuric acid or mixtures of aluminium halide and the corresponding hydrogen halide, alkanes isomerize forming more highly branched alkanes, e.g.:

$$CH_3-CH_2-CH_2-CH_3 \xrightarrow{AlBr_3+HBr} CH_3-\underset{\displaystyle CH_3}{\overset{|}{C}}H-CH_3$$

This reaction is of great importance at present, because it yields a valuable motor fuel.

*n*-Butane will isomerize into isobutane only in the presence of traces of alkene, oxygen or water [42].

Evidently, these impurities participate in the initial formation of small quantities of secondary *n*-butyl bromide according to one of the following schemes:

(a) $$CH_3-CH_2-CH=CH_2+HBr \rightleftarrows CH_3-CH_2-\underset{\displaystyle Br}{\overset{|}{C}}H-CH_3$$

(b) $$AlBr_3+O_2 \rightleftarrows AlOBr+Br_2$$

$$CH_3-CH_2-CH_2-CH_3+Br_2 \longrightarrow CH_3-CH_2-\underset{\displaystyle Br}{\overset{|}{C}}H-CH_3+HBr$$

(c) $AlBr + H_2O \rightleftarrows HOAlBr_2 + HBr$

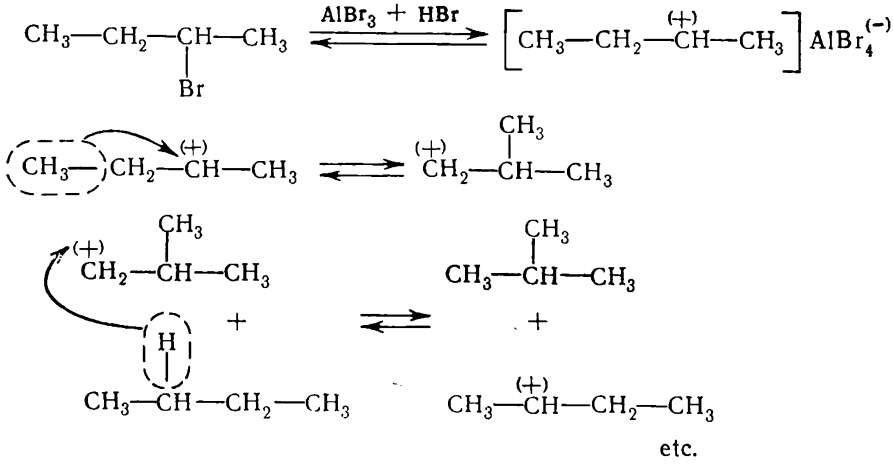
$CH_3-CH_2-CH_2-CH_3 + HOAlBr_2 \rightleftarrows$

$\rightleftarrows CH_3-CH_2-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_3 + [HOAlBrH] \longrightarrow AlOBr + H_2$

The proposed mechanism is supported by the fact that bromine is formed during the reaction of aluminium bromide with oxygen.

That the catalytic activity in reactions (c) is due mainly to the bromine atom and not to the hydroxyl follows from the observation that although $DOAlBr_2$ exchanges deuterium for the hydrogen of *n*-butane, the rate of this exchange is not proportional to the rate of isomerization.

After the preliminary formation of secondary *n*-butyl bromide the isomerization reaction proceeds as a chain process with the participation of carbonium ions.

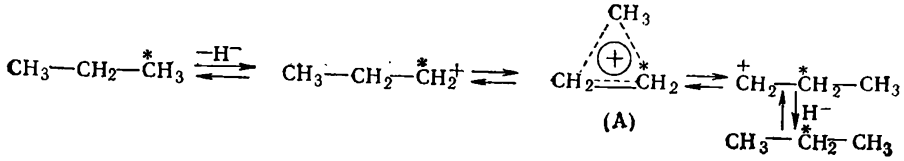



It is interesting to note that isomerization takes place even in the case of propane. Thus, after contact with aluminium bromide propane molecules containing a primary $C^{13}$ carbon atom rearrange into molecules of propane in which the $C^{13}$ occupies the central position [43]:

$$CH_3-CH_2-\overset{*}{C}H_3 \xrightarrow{AlBr_2} CH_3-\overset{*}{C}H_2-CH_3$$

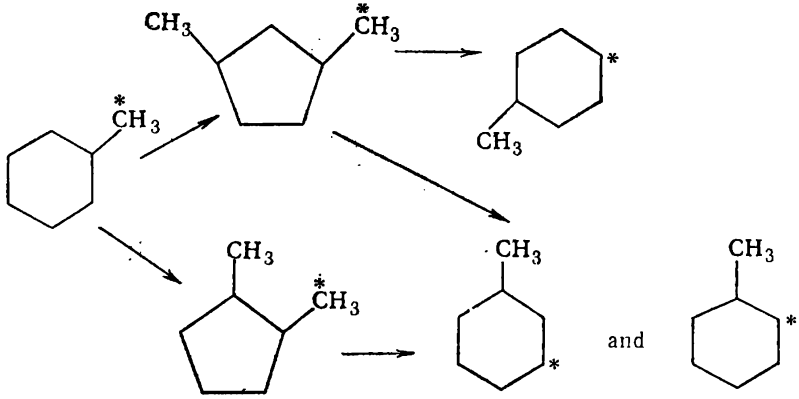
This rearrangement is intramolecular in nature because no molecules having more than one atom of $C^{13}$ are formed in it.

Apparently the isomerization in question takes place through the simplest non-classical cation (A)

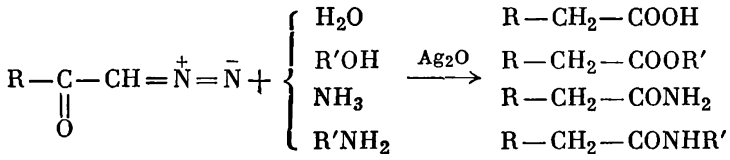


Roginsky and Sakharov [44] showed that methylcyclohexane labeled with $C^{14}$ at the methyl group isomerizes so that the labeled carbon enters the ring (the distribution of radioactivity in the ring was not studied).

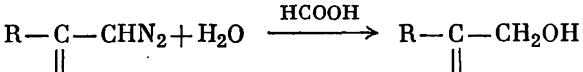
The following is a possible reaction mechanism:



**Wolf Rearrangement** [47]. The transformation of diazomethylketones under the action of water, alcohols, ammonia, and amines into acid derivatives is generally called *Wolf rearrangement.* The reaction takes place in the presence of silver oxide.



The action of water and formic acid on diazoketones in the absence of catalyst results in the formation of hydroxymethylketones as by-products.



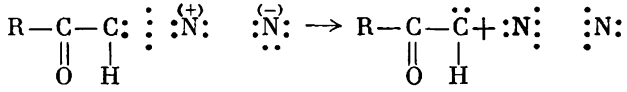
As α-diazoketones are generally prepared by the action of diazomethane on acid chlorides, the Wolf rearrangement is a stage in the

synthesis of higher acids from their lower homologues after Arndt and Eistert [48]:

$$R-COOH \longrightarrow R-COCl \longrightarrow R-CO-CHN_2 \longrightarrow HO_2C-CH_2-R$$

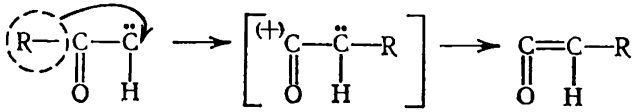
The Wolf rearrangement, apparently, proceeds according to the following mechanism.

An intermediate biradical is formed as a result of the elimination of nitrogen from the diazomethylketone. The elimination of nitrogen is caused by heat or a catalyst.



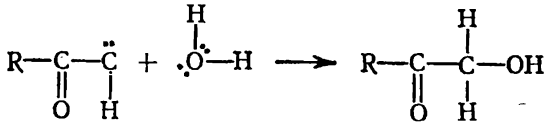
The biradical formed must be similar to a carbonium ion, because there are only six electrons in the outer electron shell of the carbon atom.

Such a biradical should undergo the usual rearrangement for carbonium ions (*a*) or should add atoms with a filled valence electron shell (*b*):



(a)

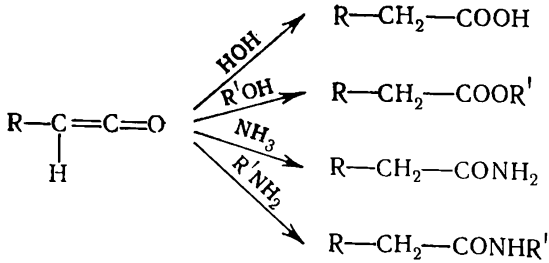
Ketene



(b)

α-Oxymethylketone

The ketene formed in reaction (*a*) naturally yields acid derivatives readily:



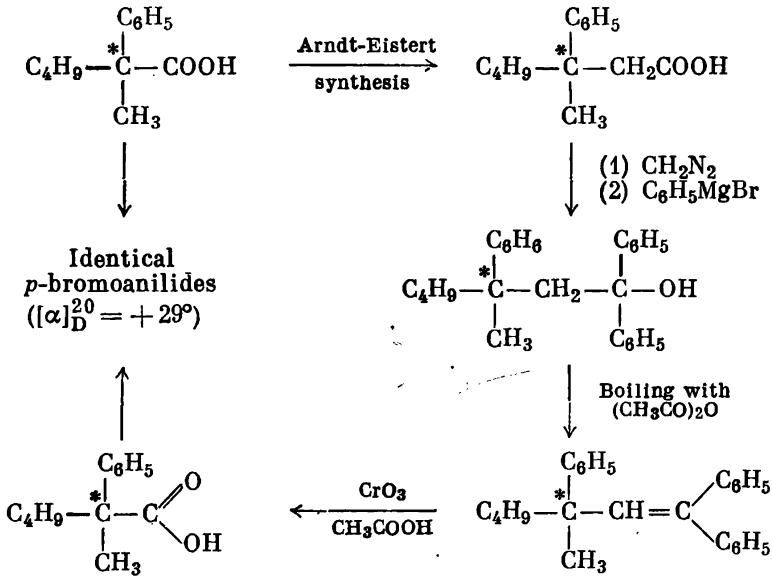

The mechanism cited is confirmed by the fact that the keten formed has been isolated in a number of cases [49].

The fact that the carbonyl group of diazomethylketone changes into the carboxyl group was established rigorously by the following sequence of reactions, carried out using a labeled carbon [50]:

$$\overset{*}{C}O_2 + C_6H_5MgBr \longrightarrow C_6H_5-\overset{*}{C}OOH \xrightarrow[(2)\ CH_2N_2]{(1)\ SOCl_2} C_6H_5-\overset{*}{C}O-CHN_2 \xrightarrow[H_2O]{Ag_2O}$$

$$\longrightarrow C_6H_5-CH_2-\overset{*}{C}OOH \longrightarrow \xrightarrow[Quinoline]{CuO\cdot Cr_2O_3} C_6H_5-COOH + \overset{*}{C}O_2$$

If the tertiary radical linked with the carbonyl group of diazomethylketone contains an asymmetric carbon atom, the Wolf rearrangement (and the Hofmann, Curtius and Schmidt rearrangements also) proceeds with retention of configuration, e.g. [51]:



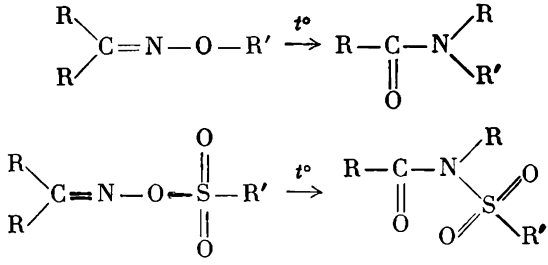

If the asymmetric atom is secondary instead of tertiary, the rearrangement proceeds with complete racemization, due, apparently, to preliminary tautomerization of the diazomethylketone on the surface of the catalyst.

**Beckmann Rearrangement** [52]. The transformation of oximes into acid amides

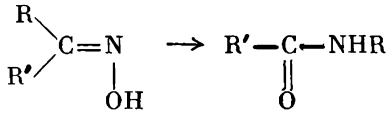
$$\begin{matrix} R \\ \diagdown \\ \quad C=N-OH \\ \diagup \\ R \end{matrix} \longrightarrow R-\overset{\overset{O}{\|}}{C}-NHR$$

was first discovered by Beckmann in 1886 [53]. It takes place under the influence of phosphorus pentachloride, phosphorus oxychloride, sulphuric acid, hydrogen chloride, acetyl chloride, benzene sulphochloride, antimony pentachloride and similar reagents.

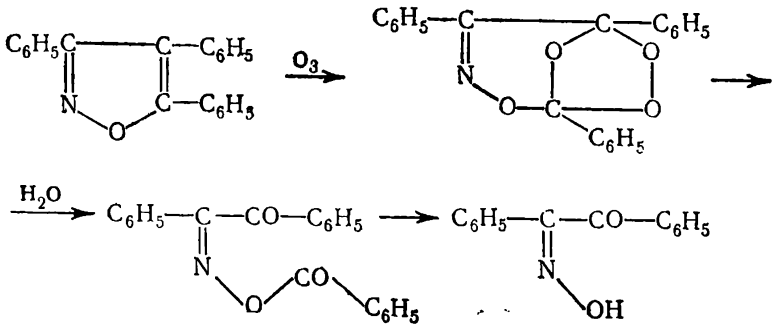
Later it was found that ethers and esters of ketoximes are also capable of rearrangement into amide derivatives.



A very interesting feature of the Beckmann rearrangement is its stereochemical specificity. In unsymmetrical ketoximes the hydroxyl group is always exchanged with the group in the *trans*-position:

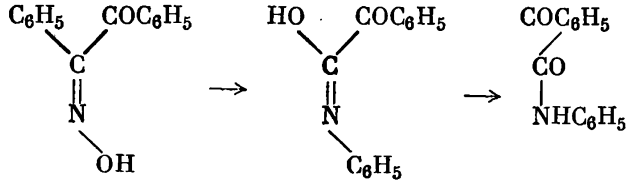


This rule was established by Meisenheimer [54]. He obtained a benzyl monoxime of known configuration by ozonolysis of triphenylisoxazole followed by hydrolysis of the ozonide formed:

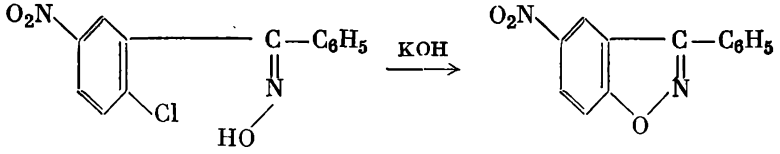


The method of obtaining this benzyl monoxime determines the *cis*-configuration of the hydroxyl group with respect to the benzoyl group.

The Beckmann rearrangement of this monoxime results in benzoyl formanilide which can form only as a result of a *trans*-rearrangement:

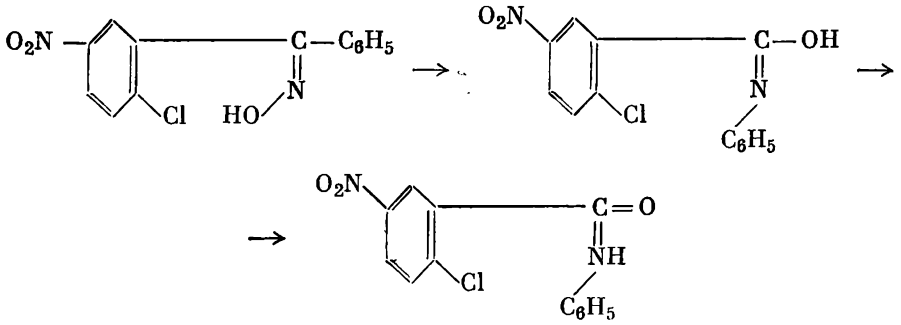


Meisenheimer gave a second proof of the *trans*-rearrangement. One of the isomers of 2-chloro-5-nitrobenzophenone oximes readily eliminates hydrogen chloride when treated with alkali, forming an isoxazole ring:



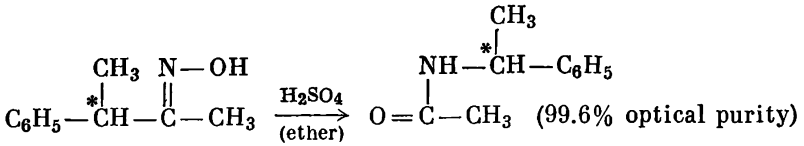
It is apparent that in this isomer the hydroxyl and the chloro-substituted benzene ring are in *cis*-configuration.

The Beckmann rearrangement of this oxime results in chloronitrobenzanilide:



i.e., in the Beckmann rearrangement the groups exchanged are in *trans*-position to each other.

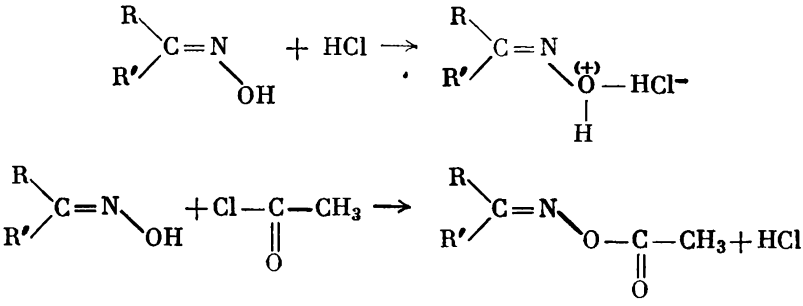
If the migrating group contains an asymmetric carbon atom, then, like in the Hoffmann, Curtius (page 578) and Schmidt (page 582) rearrangements, configuration is fully retained, e.g.:



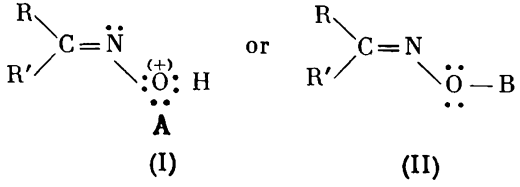
The problem of the mechanism of the Beckmann rearrangement is quite complex. Since the rearrangement is caused by such different reagents as phosphorus pentachloride, benzene sulphochloride, sulphuric acid, chloral, etc., it is rather improbable that the reaction passes through the same intermediates in all the cases. The presence of acidic catalysts is not essential, because benzophenone oxime, for example, suffers rearrangement under the influence of benzene sulphochloride and an alkali. Beckmann rearrangements are known to occur in the absence of catalysts. Thus, oxime picrates rearrange on heating.

The general mechanism of the Beckmann rearrangement may at present be represented as follows.

In the first step of the reaction the oxime hydroxyl group reacts with the catalyst, e.g.:



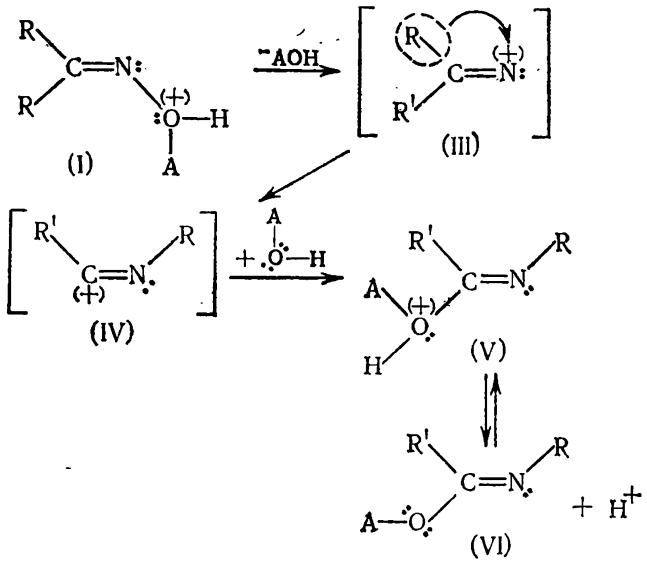
This results in intermediate substances of the general type:



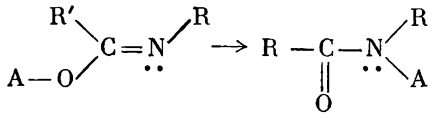
Intermediate I forms if the reaction takes place in the presence of acid. Substance II may arise under conditions favourable for the formation of ethers or esters.

Elimination of A : $\ddot{O}$ — H or : $\ddot{O}$ — $B^{(-)}$ gives cation (III), in which nitrogen has 6 valence electrons. This process is accompanied by a shift of the group R from the carbon to the nitrogen, resulting in the carbonium ion (IV). The latter adds an HOA molecule, yielding the oxonium cation (V); this loses a proton and forms an enol-

form derivative of the amide (VI):



If AOH is a strong acid, the latter compound is unstable and ketonizes spontaneously:



(VI)

The series of rearrangement steps probably proceeds continuously, as a single process. Thus, cation IV forms, apparently, from the initial substance I at such a rate that cation III does not form as a kinetically independent particle.

Exchange of AOH for a group in the *trans*-position is apparently due to the same causes as *trans*-elimination reactions in general (see page 196 *et seq.*).

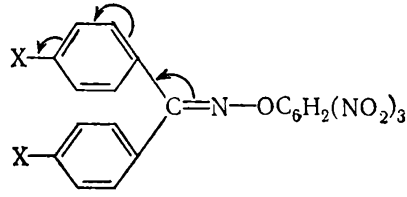
Brodsky and Miklukhin showed [55] that the Beckmann rearrangement as a whole is not an intramolecular process.

They studied the transformation of benzophenone oxime into benzanilide under the influence of phosphorus pentachloride, followed by treatment with water enriched with heavy oxygen $O^{18}$, and found that all the initial oxygen of the oxime was replaced in the anilide by the heavy oxygen of the water. It follows that the Beckmann rearrangement does not proceed by intramolecular exchange

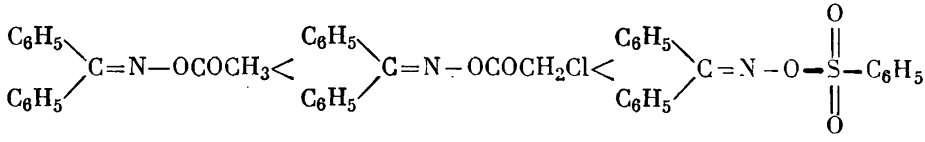
of oxygen and the phenyl group, but through intermediate stages, including removal and addition of oxygen (in the AOH molecule) as is indicated in the reaction mechanism given above.

The general mechanism is in agreement with the majority of facts known about the Beckmann rearrangement. It is a first-order reaction. It is accelerated by heating. As would be expected in a heterolytic process proceeding under the influence of electrophilic reagents, it is accelerated by polar solvents [56] or facilitated by an increase in the acidity of the solution [57]. On the other hand, irradiation has no effect on the rearrangement.

If the benzophenone part of benzophenone oxime picrate contains electron-attracting groups, the rearrangement proceeds more slowly [58], because the first stage of the reaction—elimination of the picryl anion accomplished by severing an electron pair from the nitrogen—is impeded.




On the other hand, it is easy to understand why the rate of rearrangement of esters increases in the series [59]:



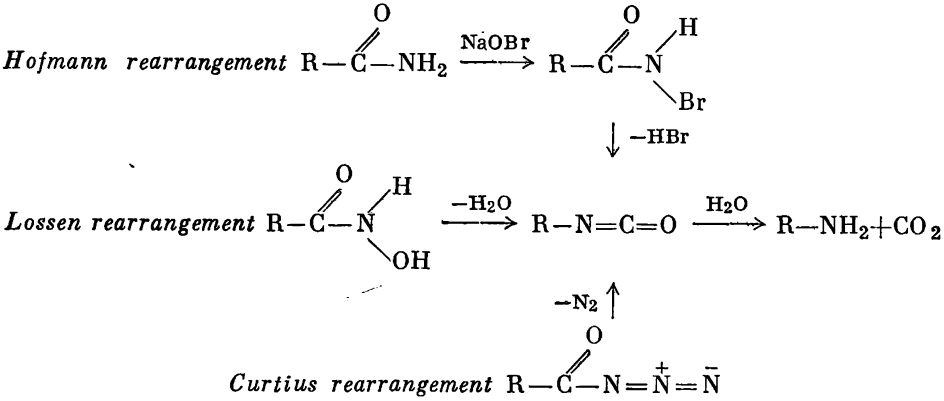

The stronger the acid, the easier its anion is eliminated from the oxime ester.

It remains, however, unclear why the curves of the rates of rearrangement under the action of hydrogen chloride are rather complex in shape [60].

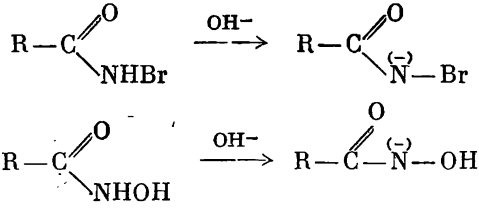
**Hofmann, Lossen and Curtius Rearrangements.** All these reactions lead to the formation of amines from amides ($RCONH_2$), hydroxamic acids (RCONHOH) or their derivatives (of the type R — CONHOX) and acid azides (R — $CON_3$).

Isocyanates are formed as intermediate products in all cases [61].

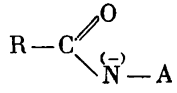
The rearrangements proceed according to the following general scheme:



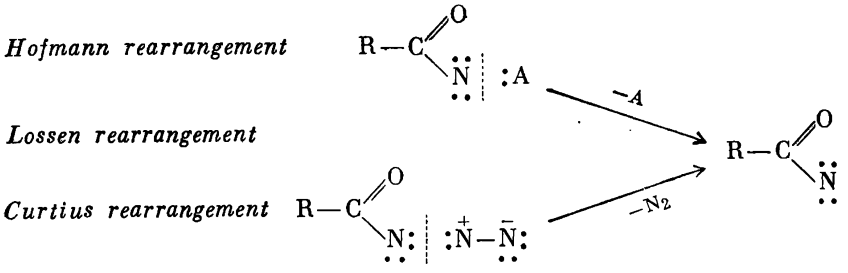

Unlike the Beckmann rearrangement, which proceeds in most cases under the influence of acidic substances, the above rearrangements take place in alkaline media. Under these conditions proton is eliminated from bromamide and hydroxamic acid:




resulting in the formation of an anion of the general formula:



In the next stage the atom or group A with a complete electronic octet splits off from the anion [62], so that the nitrogen is left with a sextet of electrons. Similarly, in the Curtius reaction a molecule of nitrogen splits off from the azide molecule.



Hauser [63] confirmed the mechanism of this stage of the reaction. He found that in the series of compounds

$$C_6H_5—CO—NH—OCOC_6H_4X$$

the Lossen rearrangement is accelerated by the electron-attracting substituents X. On the other hand, the substituents X were found to have quite the opposite influence in the rearrangement of hydroxamic acids

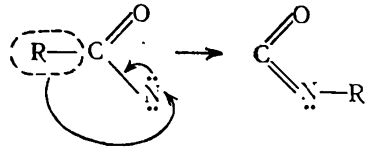
$$X—C_6H_4—\underset{\underset{O}{\|}}{C}—NH—OCOC_6H_5$$

after Lossen and bromamides

$$X—C_6H_4—\underset{\underset{O}{\|}}{C}—NH—Br$$

after Hofmann. In these cases the rate of rearrangement decreases with increasing electron-attracting properties of the substituents X.

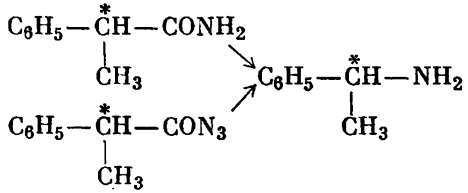
The final stage of the rearrangements under consideration consists in the migration of group R from the carbon to the nitrogen, resulting in the formation of isocyanates:



It has been suggested [64] that the group R passes over to the nitrogen with an electron pair.

It is interesting that if R is an optically active group linked with the rest of the molecule through an asymmetric carbon atom, the optical activity of R is fully retained in the Hofmann, Lossen and Curtius rearrangements (see also Schmidt's rearrangement, page 582).

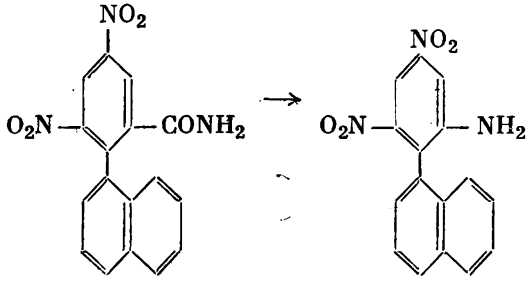
Thus, almost quantitative retention of optical activity was observed in the rearrangement of the amide and hydrazide of hydratropic acid [65]:



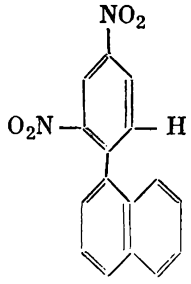
Complete lack of racemization was proved in the Curtius, Hofmann and Lossen rearrangements of optically active derivatives of benzylmethylacetic acid [66]. The amines obtained from the azide, the bromamide and from hydroxamic acid were of identical rotatory power.

All these, and a number of other factors are generally accepted as proof that the anion $R^{(-)}$ does not exist as a kinetically independent particle and that group R is transferred from the carbon to the nitrogen intramolecularly. However, if it is supposed that the free electron pair is capable of fixing the configuration of the asymmetric carbon atom (page 158), as is known to be the case with the sulphur atom, the stereochemical facts given above cannot be considered strict proof of the intramolecular course of the last stage of the rearrangements. There are, however, more reliable facts that favour the intramolecular nature of the last stage.

For instance, the Hofmann rearrangement of 3,5-dinitro-2-(α-naphthyl)-benzamide (where optical activity is due to the inhibited rotation along the bond between the benzene and naphthalene rings) results in an optically active amine of the same configuration as the initial substance [67]:




Since the compound:



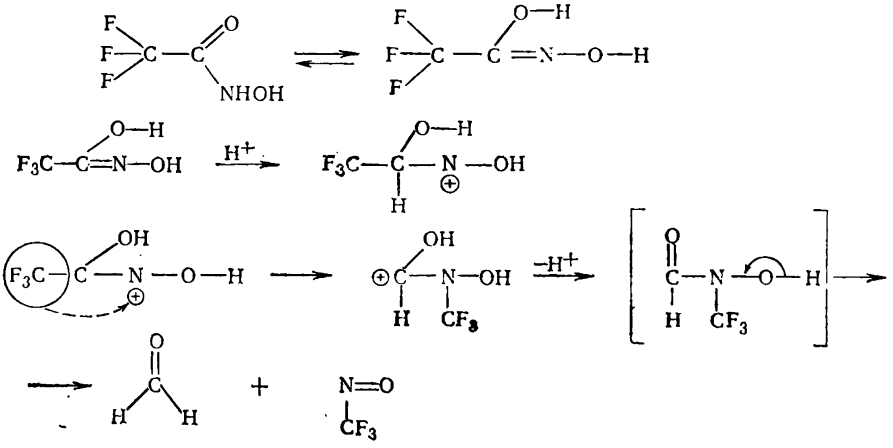

has no optically active isomers, it is evident that hydrogen has no restraining effect on free rotation. There is even less reason to believe that a free pair of electrons would restrain free rotation. Thus, if the Hofmann rearrangement in this case were not intramolecular, one should have expected racemization to occur.

Knunyants [68] discovered an interesting rearrangement, which takes place when trichloroacetohydroxamic and trifluorohydroxamic acids are heated. Trihalonitrosomethanes are obtained in high yields:

$$X_3C-\underset{\underset{O}{\|}}{C}-NH-OH \xrightarrow{t^\circ} X_3C-N=O+CH_2O$$

Owing to the high electronegativity of the trihalomethyl group the mechanism of this rearrangement differs considerably from the usual Lossen rearrangement, being apparently of the nucleophilic rather than electrophilic type.

According to Knunyants its mechanism may be expressed as follows:



**Schmidt Rearrangement.** The reaction of acids, aldehydes and ketones with an equimolecular quantity of hydrazoic acid in acid solution is called the Schmidt rearrangement or Schmidt reaction.

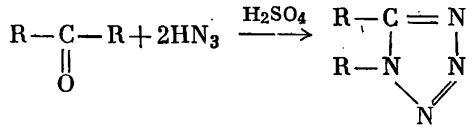
The reaction proceeds according to the schemes:

$$R-COOH+HN_3 \xrightarrow{H_2SO_4} R-NH_2+CO_2+N_2$$

$$R-\underset{\underset{H}{\diagdown}}{\overset{\overset{O}{\diagup}}{C}} +HN_3 \xrightarrow{H_2SO_4} R-C\equiv N \quad \text{and} \quad R-NH-\underset{\underset{O}{\|}}{C}-H$$

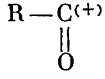
$$R-\underset{\underset{O}{\|}}{C}-R+HN_3 \xrightarrow{H_2SO_4} R-\underset{\underset{O}{\|}}{C}-NHR+N_2$$

In an excess of hydrazoic acid, substituted tetrazoles are formed from aldehydes and ketones:

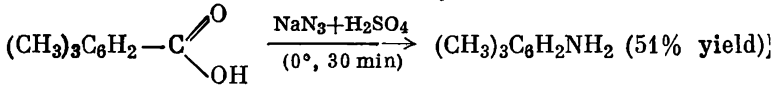


The mechanism of the Schmidt reaction is close to that of the Curtius reaction.

The Schmidt rearrangement proceeds faster if the acids dissociate in sulphuric acid to form a stable acyl cation:

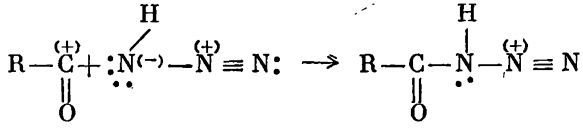


Thus, 2,4,6-trimethylbenzoic acid, which gives a stable trimethylbenzoyl cation (cf. page 422) undergoes rearrangement at 0°.



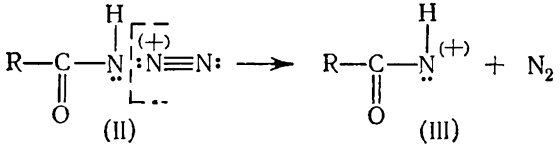
Under these conditions benzoic acid yields only traces of aniline.

In connection with this it was assumed [69] that the first stage of Schmidt's reaction consists of the addition of a molecule of hydrazoic acid to the acyl cation (I).



(I) (II)

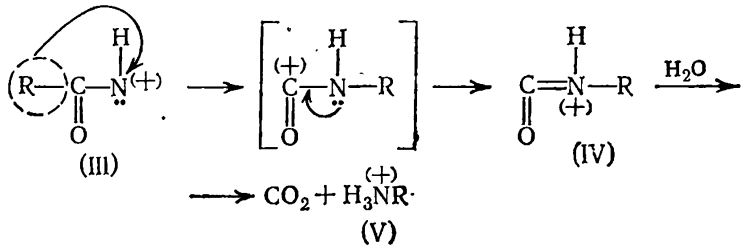
The intermediate compound (II) then loses nitrogen, resulting in the formation of cation (III) with six valence electrons on the nitrogen atom:



(II) (III)

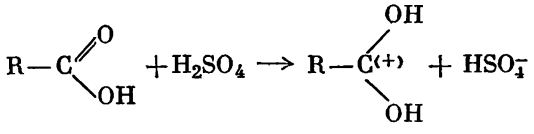
Rearrangement of cation (III) leads to the formation of the protonated form of isocyanate (IV) which is hydrolyzed to the amine

salt (V) and carbon dioxide:



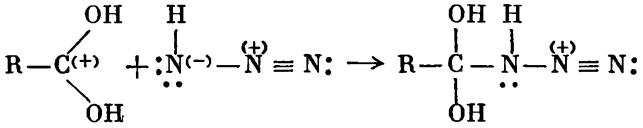
(III) (IV) (V)

In the case of acids such as benzoic a dihydroxy carbonium ion (VI) forms at first under the action of sulphuric acid:



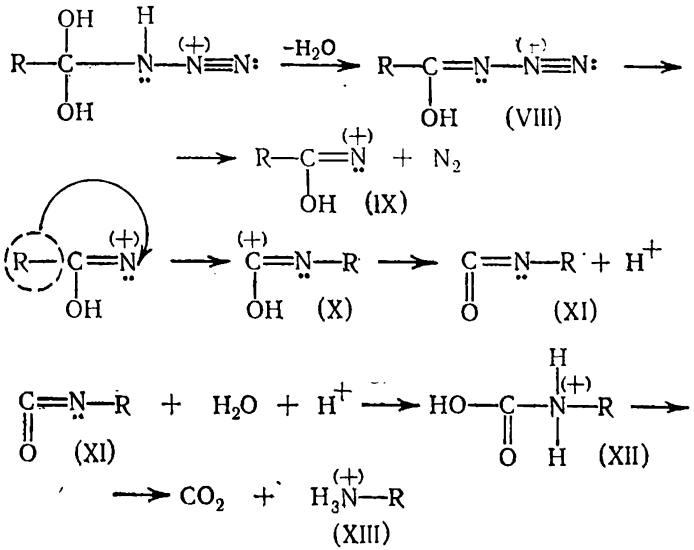
(VI)

which adds a molecule of hydrazoic acid, yielding (VII):



(VII)

After this apparently dehydration takes place, followed by nitrogen elimination and rearrangement:



(VIII) (IX) (X) (XI) (XII) (XIII)

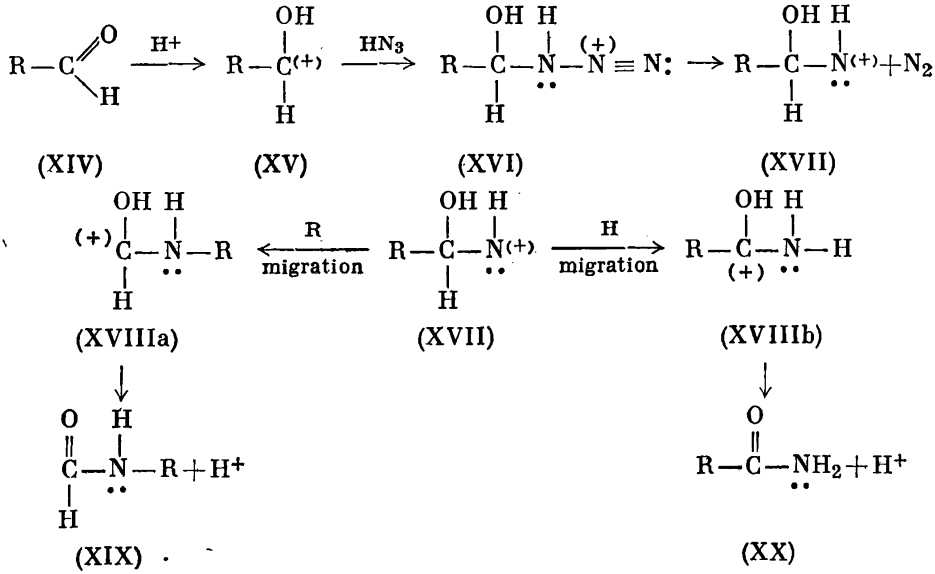
The facts are found to be in agreement with the mechanism of Schmidt's reaction.

The intermediate compounds (II) and (VIII) are two possible cations, which may result when acid azides are dissolved in sulphuric acid. The intermediate compounds (IV) and (X) are two possible cations, which may result when isocyanate is dissolved in sulphuric acid. Confirmation of the existence of the latter intermediates is the fact that phenyl isocyanate decomposes immediately in sulphuric acid to form aniline.

As in the case of the Wolf, Hofmann, Curtius, Lossen and Beckmann rearrangements (pages 571, 573, 578), the stereochemical configuration of the asymmetric carbon atom combined with the carbonyl group is retained in the Schmidt rearrangement [70].

In full agreement with the above reaction mechanism is the fact that the rate of nitrogen elimination increases with increasing electron-donor properties of the group R [71]. This indicates that the decomposition of azides is a slow stage of the Schmidt reaction.

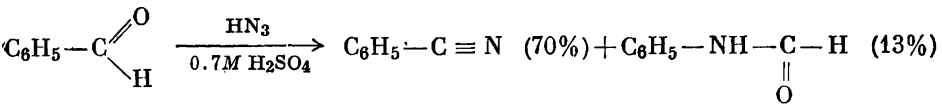
The mechanism given above also explains the formation of amides from carbonyl compounds, though the interpretation is more complex in this case. The Schmidt reaction with aldehydes may be represented by the following scheme:




This scheme, however, is not quite satisfactory. According to it formamide (XIX) and amide (XX) should form, whereas actually formamide (XIX) and a nitrile are formed.

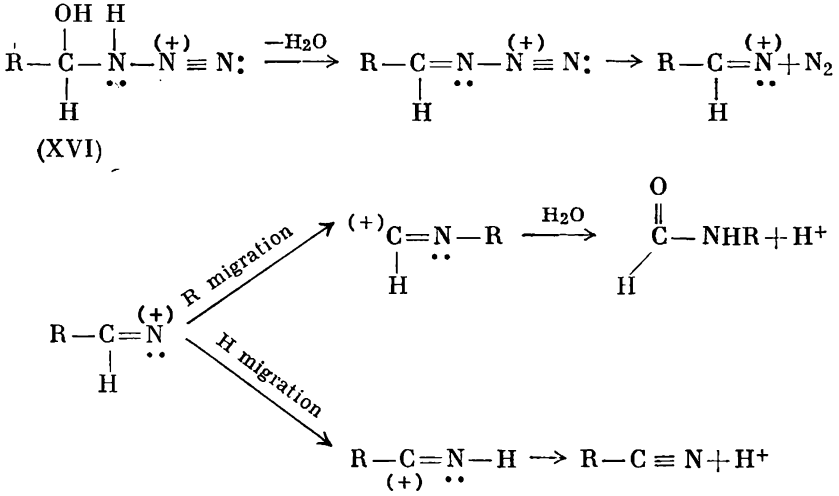
Thus, when benzaldehyde is treated with hydrazoic acid and small amounts of sulphuric acid the predominant reaction product is the

nitrile:



In the presence of a large excess of sulphuric acid the main reaction product is an anilide.

These facts can be explained by a hypothesis according to which adducts of hydrazoic acid to the carbonyl compound (XVI) like the adduct of hydrazoic acid to acids (VII) is first dehydrated, and undergoes rearrangement only after this:



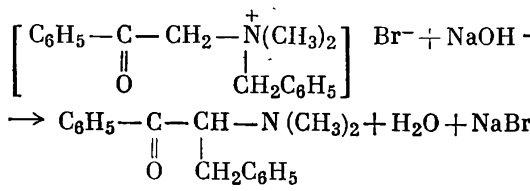
A comparison of the Hofmann, Lossen, Curtius, Beckmann, Schmidt (and Wolf) rearrangements shows that they resemble each other and are very close in mechanism.

### 9-1.3 Electrophilic Rearrangements in the Aliphatic Series

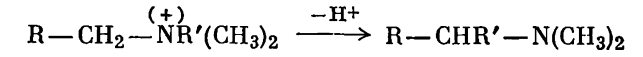
Electrophilic (or cationotropic) rearrangements are those in which groups with a shortage of electrons migrate to atoms carrying a negative charge or an unshared pair of electrons. As before (page 549), aliphatic systems will include saturated as well as unsaturated and aromatic molecules, in the rearrangements of which the multiple bonds do not play a determining part.

**Stevens Rearrangement.** Stevens *et al.* [72] discovered that in alkaline solution benzyl and certain other groups are capable of migrating from the nitrogen atom of the quaternary ammonium salt to the neighbouring carbon atom.

At first the reaction was studied on the following example:



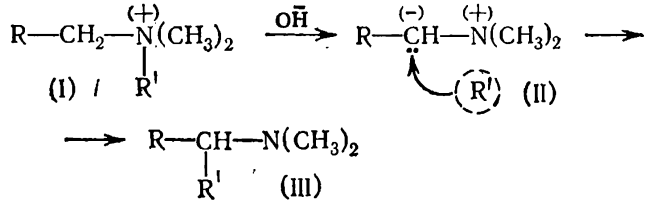
The general scheme of the rearrangement is:



The rearrangement was studied in the case of such quaternary ammonium salts where R = acetyl, benzoyl, substituted benzoyl, vinyl, phenyl, and R′ = benzyl, substituted benzyl, α-phenylethyl, benzhydryl, 9-fluorenyl, phenacyl.

The reaction is monomolecular. All attempts to find exchange products between two different quaternary ammonium salts were unsuccessful which points to the intramolecular character of the rearrangement.

The mechanism of the rearrangement may be represented as follows. The hydroxyl ion removes the mobile α-hydrogen atom in the initial compound (I), resulting in the carbanion (II). In the latter, the group R′ passes over as a cation to the carbon atom carrying a negative charge. This results in the formation of the final amine (III):



It was established that the power of substituents in the group R′ (benzyl) to increase the rate of rearrangement rises with their electron-attracting properties:

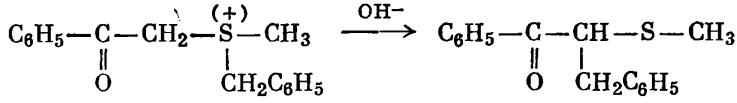
$$CH_3O < H, \quad CH_3 < Cl, \ Br, \ I < NO_2$$

These facts are easy to correlate with the above reaction mechanism, if it is assumed that the group R′ with its sextet of electrons begins to form a bond with a negatively charged carbon atom before its old bond with the nitrogen atom is broken.

Substituents in the group R, on the contrary, slow down the reaction more and more as their electron-attracting properties

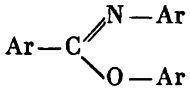
increase. This dependence is not surprising because electronegative substituents impede migration of the group R′ by attracting the free electron pair in the carbanion (II).

A quite analogous rearrangement occurs in sulphonium compounds [73]:

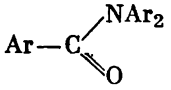


Oxonium compounds are incapable of such a rearrangement.

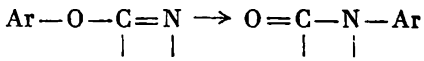
**Rearrangement of Imido-Esters and Amidines.** When heated above 220° imido-esters of the aromatic series



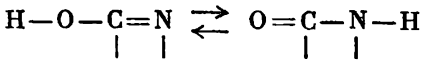
isomerize into diaryl acid amides:



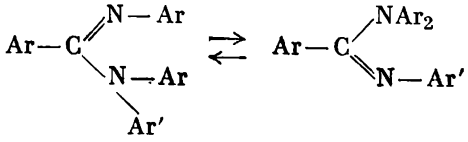
i.e., the aryl group attached to the oxygen migrates to the nitrogen



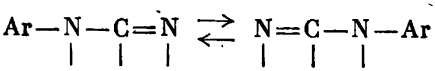
like a proton migrates in a tautomeric amide-imide system:



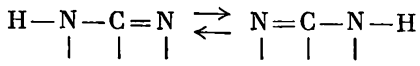
Compounds of the amidine series behave similarly:



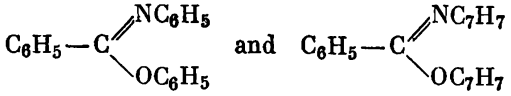
In this case the aryl group migrates from one nitrogen atom to the other



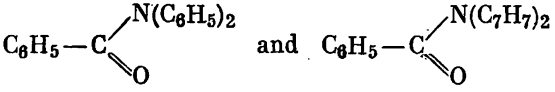
The process is reversible, as in the case of the corresponding tautomeric system:



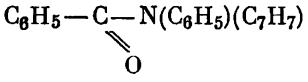
These reactions are monomolecular [74]. Their intramolecular nature can be proved by heating a mixture of two different imido-esters (or amidines) at a temperature high enough to cause rearrangement. Under these conditions, for example, the imido-esters:



yield two substances:



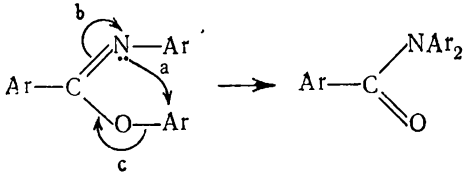
but yield no traces of the mixed product:



Thus, it is evident that the migrating groups migrate within the molecule and do not become free, kinetically independent, particles for any time interval (in distinction to prototropic* transformations in the same systems).

Like in the Stevens rearrangement, electronegative substituents in the migrating group facilitate rearrangement and the same substituents in other aryl groups impede the reaction.

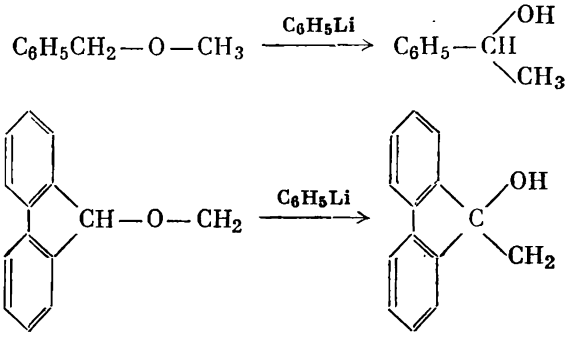
The rearrangement probably begins with the formation of a bond between the Ar group migrating with a sextet of electrons, and the nitrogen atom. The bond is formed through the free electron pair of the nitrogen (process *a*) after which electron shifts (*b* and *c*) take place, resulting in the final product:



**Wittig Rearrangement.** The Wittig rearrangement consists in the conversion of ethers into alcohols under the influence of phenyl

* Prototropic transformations are processes involving proton transfer.

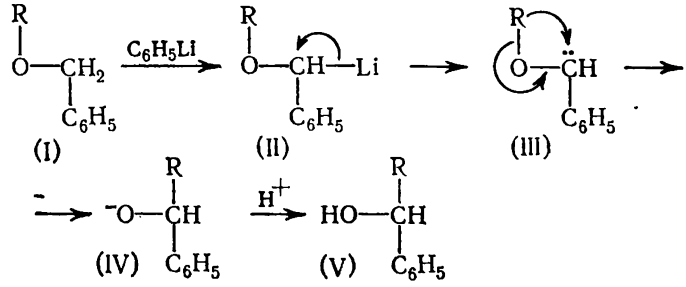
lithium [75], e.g.:



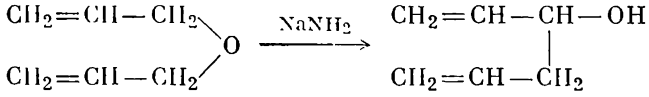
The mechanism of the rearrangement is described below. Initially, lithium apparently replaces the α-hydrogen atom of the benzyl or some other reactive group (I).

Then the organolithium compound (II) or the carbanion (III) readily formed from it undergoes rearrangement.

The group attached to the oxygen transfers with a sextet of electrons to the carbon atom possessing a free electron pair, resulting in the formation of anion (IV) which adds a proton to form the end product, an alcohol (V):



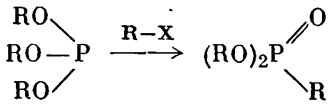
The Wittig rearrangement has also been carried out with the aid of sodamide in liquid ammonia [76]:



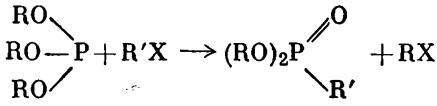
This fact is fully in agreement with the mechanism of the rearrangement given above.

**Arbuzov Rearrangement.** The Arbuzov rearrangement consists in the isomerization of esters of phosphorous acid into esters of

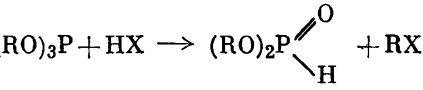
alkylphosphonic acid under the influence of alkyl halides [77]:



If esters of phosphorous acid are treated with alkyl halides (containing other groups than those in the esters treated) the corresponding alkylphosphonic esters result.

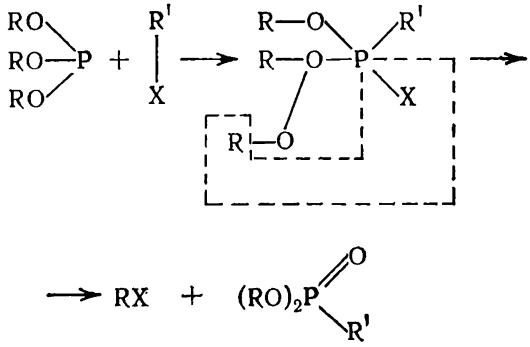


The reaction also proceeds under the influence of hydrogen halides:



The Arbuzov rearrangement is widely used for the synthesis of organophosphorus compounds [78]. Its mechanism, however, has not been studied sufficiently well.

In general, this reaction is usually portrayed by the following diagram:

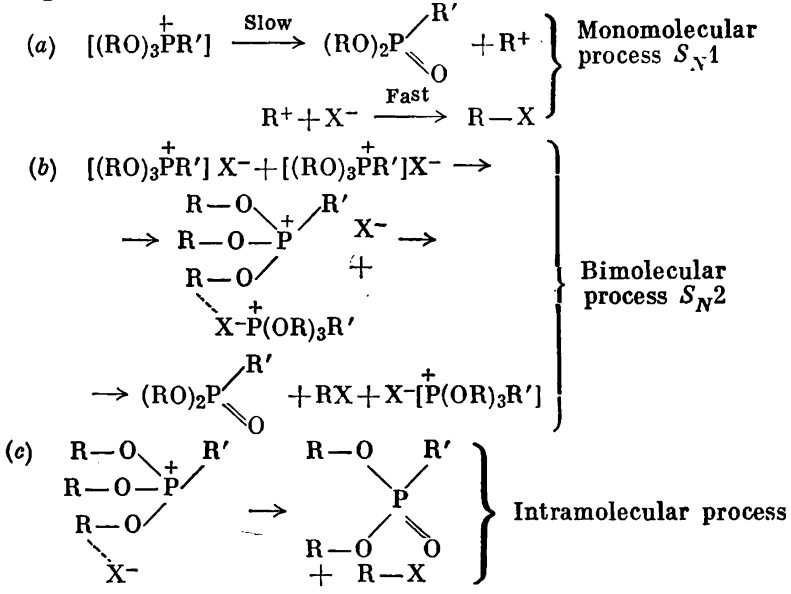


This concept of the course of the reaction is confirmed by the formation of a stable addition product of methyl iodide to triphenyl phosphite which yields diphenyl methylphosphonate on thermal decomposition.

The addition product of alkyl halide to phosphorous acid esters is probably an ionic type compound $[(RO)_3P^+R']X^-$; the further course of the rearrangement consists in migration of the group R as a cation from the oxygen to the anion X.

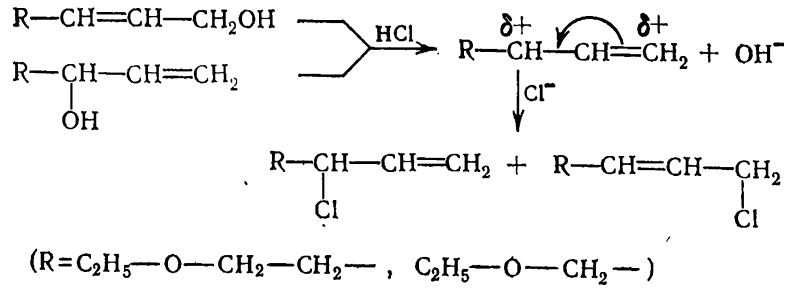
It has been suggested that depending on the structure of the group R and the reaction conditions this process may proceed by one of the

following three mechanisms:




To decide which of these three mechanisms is the one by which the rearrangement proceeds, the reactions of hydrogen halides and alkyl halides with optically active phosphorous acid esters (obtained from optically active alcohols) were studied. As a result of the action of hydrogen chloride and ethyl iodide upon tri-(2-octyl)-phosphite, obtained from (+)-octanol-2, inverted (—)-2-chloro- and (—)-2-iodooctanes are formed [79]. The fact of inversion is an indication of the bimolecular nature of these reactions.

Pudovik [80] investigated reactions of alkyl halides and hydrogen halides with phosphorous acid esters containing unsymmetrical allyl groups. He proceeded from the fact established by him, that the action of hydrogen chloride on isomeric primary and secondary ethoxypentenols and butenols, which yield identical carbonium ions in reactions proceeding according to an $S_N1$ mechanism, results in mixtures of isomeric chlorides of the same composition:



Reactions of phosphorus trichloride with the following alcohols were studied:

$C_2H_5-O-CH_2-CH_2-CH=CH-CH_2OH$, $C_2H_5OCH_2CH_2CHOHCH=CH_2$, $C_2H_5-O-CH_2-CH=CH-CH_2OH$ and $C_2H_5-O-CH_2CHOH-CH=CH_2$.

It was shown that isomeric alcohols yield mixtures of primary and secondary chlorides which differ considerably from each other in composition. At the same time, mixtures of chloro derivatives obtained by the action of $PCl_3$ on secondary ethoxypentenols and ethoxybutenols are very close in composition to the mixtures of chloro derivatives formed in the reaction of isomeric ethoxypentenols and ethoxybutenols with hydrogen chloride.

These results suggest that the reaction of chlorine anions with the primary allylic radicals contained in the positively charged ion $[(RO)_3PR']^+$ proceeds predominantly according to a bimolecular mechanism; the latter may be represented by the following diagram:

$$PCl_3 + 3HO-CH_2-CH=CH-R \longrightarrow (R-CH=CH-CH_2O)_3P + 3HCl$$

$$(R-CH=CH-CH_2O)_3P + HCl \longrightarrow (R-CH=CH-CH_2O)_2\overset{+}{P}\overset{H}{\diagup} \longrightarrow$$

$$Cl^- \cdots CH_2-O \diagup$$

$$CH=CH-R$$

$$\longrightarrow (R-CH=CH-CH_2O)_2P\overset{O}{\diagup\!\!\diagdown}\underset{H}{} + R-CH=CH-CH_2Cl$$

$(R=CH_3,\ C_2H_5OCH_2CH_2)$

In the case of secondary ethoxypentenol and butenol the last stage of the reaction (Arbuzov rearrangement) proceeds, apparently, almost wholly according to a monomolecular mechanism $S_N1$, which may be represented as follows:

$$PCl_3 + 3R-CHOH-CH=CH_2 \longrightarrow$$

$$\longrightarrow (CH_2=CH-CHRO)_3P + 3HCl$$

$$(CH_2=CH-CHRO)_3P + HCl \longrightarrow$$

$$\longrightarrow (CH_2=CH-CHRO)_2\overset{+}{P}\overset{H}{\diagup}$$

$$CH_2=CH-CHRO \diagup \quad Cl^- \longrightarrow$$

$$\longrightarrow (CH_2=CH-CHRO)_2P\overset{H}{\diagup\!\!\diagdown}\underset{O}{} + \overset{\delta+}{CH_2}=CH-\overset{\delta+}{CHR}$$

$$\longrightarrow (CH_2=CH-CHRO)_2POH + R-CH=CH-CH_2-Cl$$

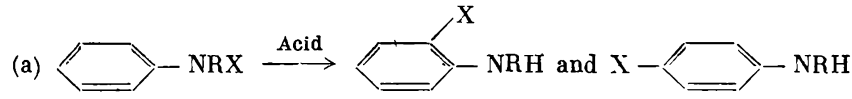
$$+ R-CHCl-CH=CH_2$$

The mechanism of the Arbuzov rearrangement needs further study. However, it is already evident that the mechanism of this reaction may differ depending on the structure of reacting substances and on the reaction conditions.

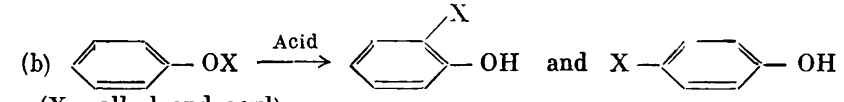
## 9-2 REARRANGEMENTS IN THE AROMATIC SERIES

A large number of examples of aromatic compounds are known where atoms or groups of atoms linked with the nitrogen or oxygen of the substituent rearrange into the *ortho-* or the *para*-position of the aromatic ring under the influence of acids. Reactions of this type are called aromatic rearrangements.

They may be summarized by the following two schemes:




(X = Cl, Br, I, $NO_2$, NO, $N_2Ar$, NRAr, Alk, OH, $SO_3H$; R = H, Alk).




(X = alkyl and acyl)

In this section aromatic electrophilic and nucleophilic inter- and intramolecular rearrangements will be considered.

### 9-2.1 Electrophilic Rearrangements in the Aromatic Series

Aromatic electrophilic (cationotropic) rearrangements include rearrangements during which the migrating group passes from the substituent to the aromatic ring as an electrophilic particle without the electrons with which it was linked to the side chain.

**Chloramine Rearrangement.** N-chloroacetanilide ($C_6H_5$—NCl—$COCH_3$) rearranges nearly quantitatively under the influence of hydrochloric acid to a mixture of *o-* and *p*-chloroacetanilides [81].

Hydrochloric acid is the only reagent which causes this rearrangement; the ratio of the *ortho-* and *para*-isomers formed is the same as on direct chlorination of acetanilide [82]. It was also established [83] that in acid aqueous solutions there is an equilibrium

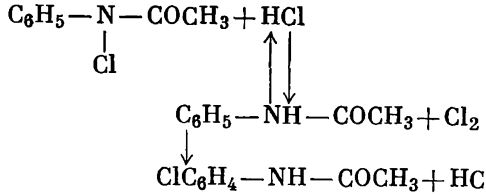
$$C_6H_5-\underset{\displaystyle Cl}{\underset{|}{N}}-COCH_3+HCl \rightleftarrows C_6H_5-\underset{\displaystyle H}{\underset{|}{N}}-COCH_2+Cl_2$$

It is apparent from these facts that the chloramine rearrangement takes place in two stages: initially, chlorine forms as a result of the reversible reaction between N-chloroacetanilide and hydrochloric

acid, and then the chlorine reacts with acetalinide, entering the aromatic ring in accordance with the rules of orientation:

$$Cl_2 + C_6H_5NHCOCH_3 \longrightarrow ClC_6H_4NHCOCH_3 + HCl$$

The process as a whole proceeds according to the following mechanism:

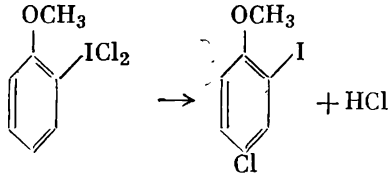


Quantitative conversion of N-chloroacetanilide into ring-substituted anilides is due to the irreversibility of chlorination in the ring.

The two-stage mechanism of the chloramine rearrangement is confirmed also by the fact that in the presence of hydrochloric acid N-chloroacetanilide is an excellent chlorinating agent for aromatic amines, anilides and phenols [84].

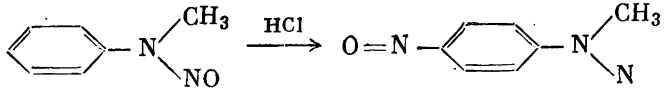
It is clear from the above that at a certain stage of the process the chlorine must be in the free state. Chloramine rearrangement is evidently an intermolecular* rearrangement.

**Rearrangement of Aryliodonium Dichloride.** Compounds of aryliodonium dichloride rearrange easily to aromatic chloroiodo derivatives, e.g.:



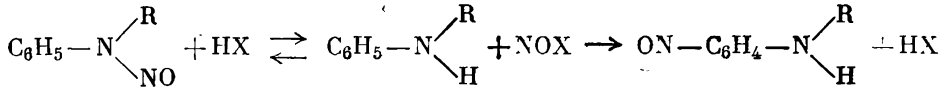
This rearrangement was proved to be *intermolecular* by chlorinating acetanilide with aryliodonium dichloride [86].

**Rearrangement of Nitrosoamines.** Aromatic nitrosoamines rearrange in the presence of hydrochloric or hydrobromic acid to isomeric reaction products with the nitroso group attached directly to the nucleus [87], e.g.:



* It is not impossible that there are conditions under which the chloramine rearrangement may proceed intramolecularly. Thus, it is possible, that the conversion of N-chloroacetanilide, N-bromoacetanilide, N-iodoformanilide and N-bromobenzanilide in non-aqueous solvents (chlorobenzene, anisole) is a one-stage intramolecular process [85].

This rearrangement is of an *intermolecular* nature and apparently proceeds as follows:

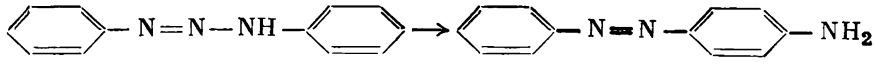


First of all, nitrosoamine splits under the influence of the acid into a secondary amine and nitrosyl halide. In the second stage of the rearrangement nitrosyl halide (or the products of its transformation) nitrosates amine into the ring.

Experimental data confirm this intermolecular rearrangement mechanism. Thus, in certain cases, when the yield of the rearrangement product was low, it could be increased by adding sodium nitrite to the reaction mixture [88]. On the contrary, when the rearrangement was carried out in the presence of urea (which binds NOX or the products of its conversion) no C-nitrosated substances formed at all; only secondary amines resulted [89].

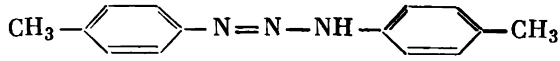
Finally, during the rearrangement the nitroso group may enter another molecule as well. For example, when N-nitroso-N-methylaniline is acted on by alcoholic hydrogen chloride in the presence of dimethylaniline, methylaniline and *p*-nitrosodimethylaniline are formed [90].

**Diazoamino-Aminoazo Rearrangement.** If diazoaminobenzene formed from phenyldiazonium chloride and aniline is heated with aniline hydrochloride it changes to *p*-aminoazobenzene.

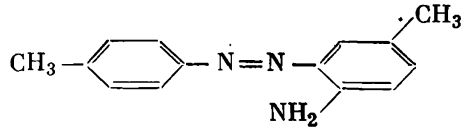


In this case the $C_6H_5-N_2$ group migrates from the nitrogen atom to the *p*-carbon atom of the benzene ring.

Diazoaminotoluene

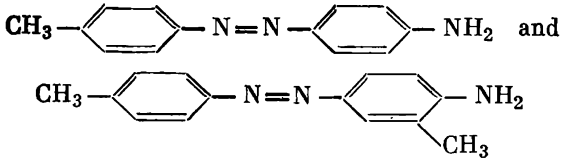


in which *p*-position is occupied changes to 4′,5-dimethyl-2-aminoazobenzene in the presence of *p*-toluidine hydrochloride in a low yield:



the migrating group $C_7H_7-N_2-$ being in the *ortho*-position to the amino group.

When diazoaminotoluene is heated with aniline or *o*-toluidine hydrochlorides, the migrating group $CH_3C_6H_4 - N_2-$ enters the aniline or *o*-toluidine nuclei, resulting in 4-methyl-4'-aminoazobenzene or 3,4'-dimethyl-4-aminoazobenzene [91]:



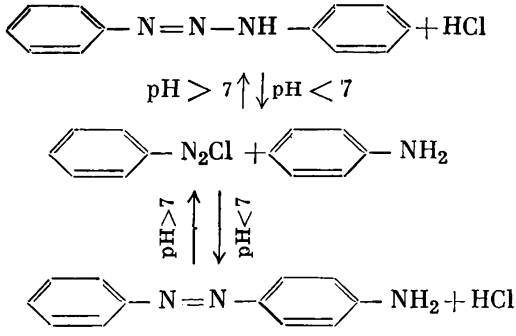

This shows that the rearrangement proceeds intermolecularly.

In studying the kinetics of the rearrangement it was established [92] that the rate of conversion of diazoaminobenzene is proportional to the concentration of aniline hydrochloride; if other salts of aniline are used instead of aniline hydrochloride, the rate of the reaction changes depending on the strength of the bound acid. It follows that free acid participates in the rearrangement.

If diazoaminobenzene is heated in acid solution with β-naphthol, aniline and the product of diazo coupling of phenyldiazonium chloride with β-naphthol (benzeneazonaphthol) can be isolated in 90% yield [93].

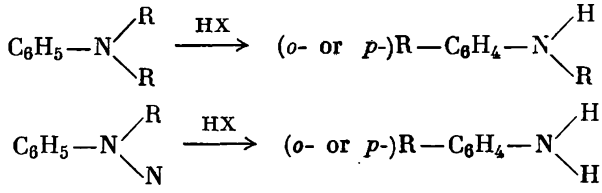
On the other hand, it was found [94] that the reaction of phenyldiazonium chloride with aniline in a neutral, weakly basic or weakly acidic medium proceeds in two independent directions, one of which results in diazoaminobenzene and the other in *p*-aminoazobenzene. Increasing the acidity favours the second direction which becomes the sole reaction after a definite concentration of the acid has been reached.

All these facts suggest that the diazoamino-aminoazo rearrangement passes through the stage of formation of aryldiazonium chloride and a free amine which then enter into the diazonium condensation reaction:



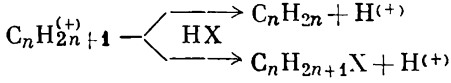
**Rearrangement of Alkylanilines.** When alkyl- or dialkylaniline hydrochlorides, hydrobromides or hydroiodides (and also phenyltrialkyl ammonium salts) are heated to 250-350°, the alkyl groups migrate into the *o*- or *p*-position of the aromatic ring [95].

The same transformation takes place when amines are heated with metallic salts, for example, with zinc chloride, cadmium chloride, cobaltous chloride:



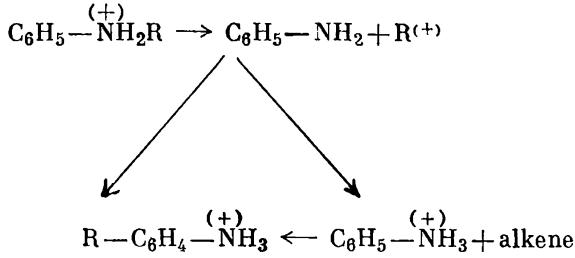
This rearrangement is of great importance, because it is an excellent method of synthesizing aniline homologues.

The reaction, evidently, begins with the splitting off of an alkyl cation [96], which then alkylates the aromatic ring. The by-products formed—alkenes and alkyl halides—are the usual products of transformation of alkyl cations:



If the alkyl groups are branched, the formation of alkene is of great significance, because the rearrangement will go further if the stage of alkylation of the aromatic ring is accomplished by an alkene [97] than when it is accomplished by a cation.

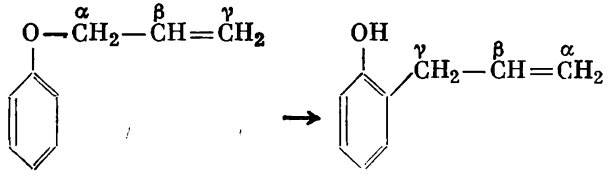
The general mechanism of the rearrangement may be illustrated by the following diagram:



The correctness of the hypothesis that there are two paths in the general case by which the rearranged product is formed has been confirmed by experiment. Thus, if methylaniline hydrobromide

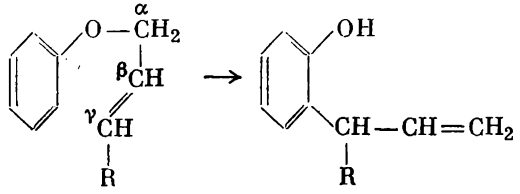
or hydroiodide is heated at 300° in an open vessel, high yields of toluidines will result, while *tert*-butylaniline hydrochloride heated at 212° (or the free base heated with cobaltous chloride) under the same conditions gives but a small yield of *p*-amino-*t*-butylbenzene, because the isobutylene which is formed in a high yield leaves the reaction mixture and does not alkylate the aromatic ring.

**Rearrangement of Alkyl-Aryl Ethers (Claisen Rearrangement).** Claisen showed [98] that when allylphenyl ethers are heated to 200° ring-allylated phenols result. The allyl group migrates from the oxygen atom to a carbon of the benzene ring, entering predominantly into the *o*-position. For instance, allylphenyl ether is transformed into *o*-allylphenol:



No *p*-allylphenol was found in this reaction. The Claisen rearrangement is a monomolecular reaction [99]. The allyl group is linked with the *o*-carbon atom of the benzene ring through its γ-carbon atom [100].

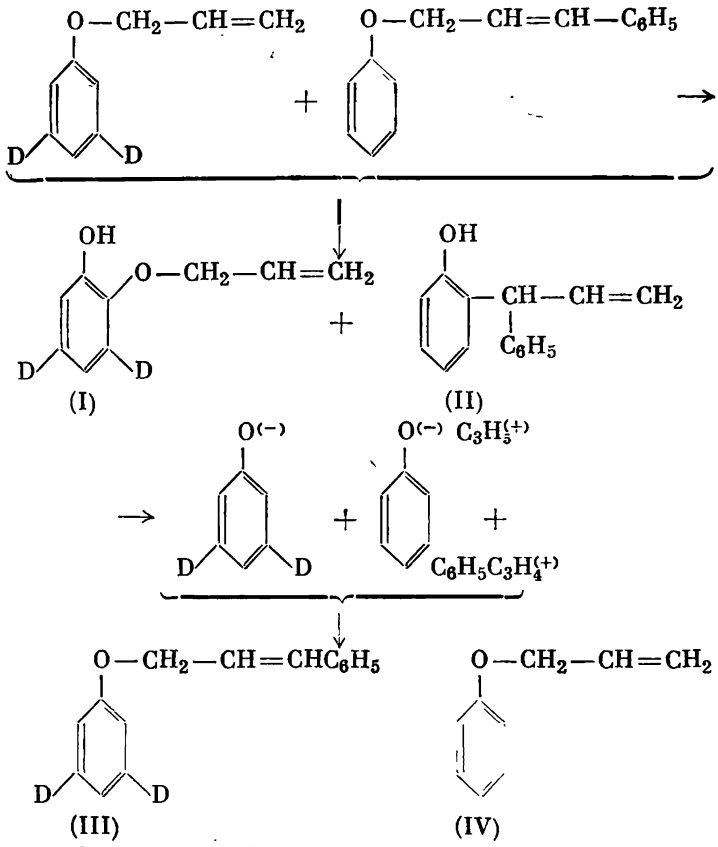
This is evident from the following rearrangement:



Migration of the allyl (or substituted allyl) group to the *o*-carbon atom is an *intramolecular* process. Thus, if a mixture of cinnamylphenyl and allyl-β-naphthyl ethers is heated, each compound rearranges independently; no substitution of the alkenyl group into the ring of the other compound took place.

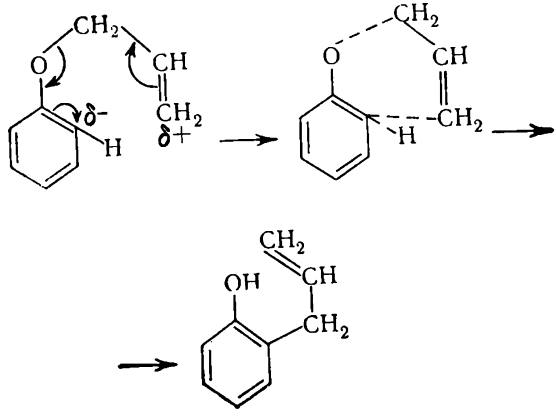
Convincing proof of the intramolecular mechanism of rearrangement of allylphenyl ethers was obtained by the isotope method [101]. Rearrangement of heavy allylphenyl ether (with deuterium in *meta*-positions) was carried out in mixture with cinnamylphenyl ether. Had the rearrangement proceeded through the stage of ion (or radical) formation, compounds (III) and (IV) would also have

formed:

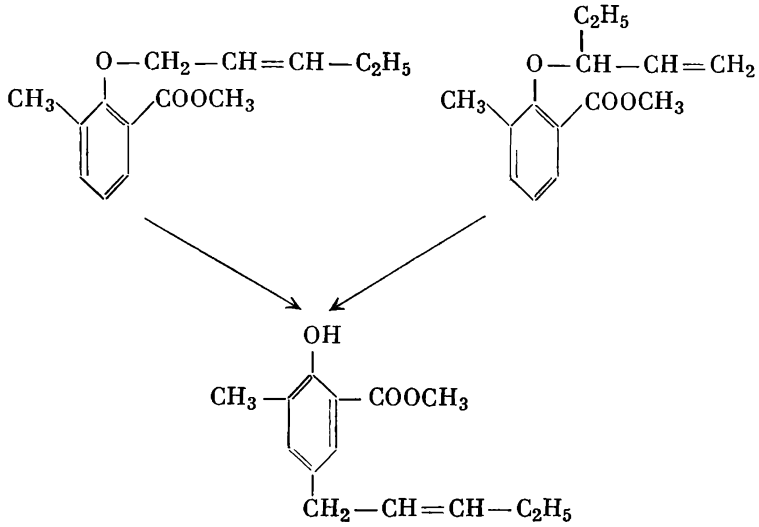



Actually, only compounds (I) and (II) result.

Thus the mechanism of rearrangement of allylphenyl ethers to *o*-allylphenols may be depicted as follows:

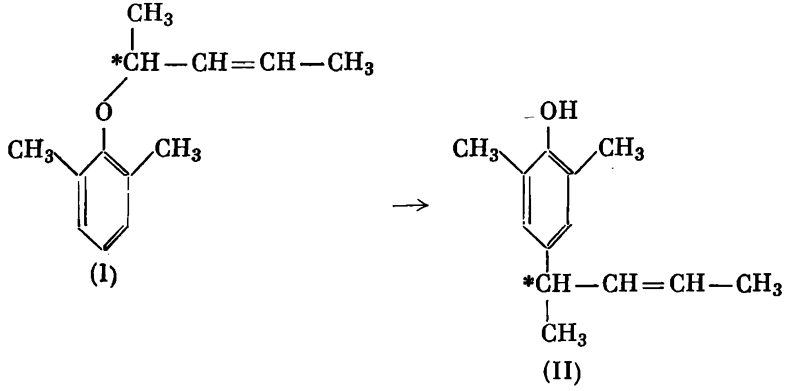


If the *ortho*-positions are occupied by substituents, the group linked with the oxygen migrates to the *p*-position [102]; however, in this case either the α- or the γ-carbon atom may link with the *p*-carbon, for example:



If the *para*- and both *ortho*-positions are occupied (as in the case of allyltrialkylphenyl ethers), heating will eliminate an alkene.

In all probability the mechanism of *para*-migration differs substantially from the mechanism of *ortho*-migration. However, there is no reason to consider this process an intermolecular one during which the alkyl group is at first completely separated from the molecule and only afterwards substitutes for hydrogen in the *para*-position. The fact that in *para*-migration the allyl (or substituted allyl) group does not react with the solvent molecule (diethyl aniline) is evidence against such a hypothesis. Rearrangement of the optically active ether (I)



(I) (II)

also results in an optically active compound (II) [103]. This shows that the bond with the *para*-carbon atom of the benzene ring begins to form before the ether linkage is broken.*

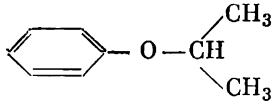
Cases are known where a tertiary alkyl or benzyl group migrates from oxygen to the *ortho*- or *para*-position of the nucleus. A new linkage is formed with the carbon atom which was bound to the oxygen [105].

Cases of migration of the benzyl group into the nucleus of another molecule are also known. Thus, if benzylphenyl ether is heated with β-naphthol, α-benzyl-β-naphthol results. If a solution of benzylphenyl ether in quinoline is heated at 250°, benzylquinolines, phenoxyquinolines, phenol and toluene [106] are formed besides the normal rearrangement products (*o*- and *p*-hydroxydiphenylmethanes).

There are numerous examples of rearrangements of alkylphenyl ethers into alkylphenols under the influence of heat and catalysts (hydrogen chloride, sulphuric acid, zinc chloride, boron trifluoride, aluminium trichloride, etc.). Under these conditions tertiary and secondary (but not primary) alkyl groups may migrate. The migrating group enters the *ortho*- or *para*-position.

A new bond is formed with the carbon atom formerly linked to oxygen. Some groups undergo isomerization in the process, for example, the isobutyl group is isomerized into *tert*-butyl.

In many cases [107] the alkyl group enters the nucleus of another molecule, for example:



$$\xrightarrow{BF_3} (o\text{- and } p\text{-})iso\text{-}C_3H_7C_6H_4OH + {}$$

$$+ C_6H_5OH + (o\text{- and } p\text{-})iso\text{-}C_3H_7C_6H_4OC_3H_7$$

$$C_6H_5{-}CH_2{-}O{-}C_6H_5 \xrightarrow[[C_6H_5OCH_3]]{ZnCl_3} (o\text{- and } p\text{-})C_6H_5CH_2C_6H_4OH + {}$$

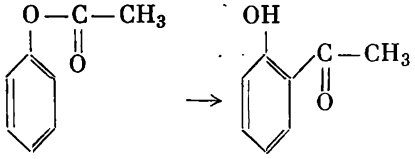
$$+ (o\text{- and } p\text{-})C_6H_5CH_2C_6H_4OCH_3$$

There is no doubt that all these catalytic as well as thermal rearrangements of benzyl- and *tert*-alkylaryl ethers are *intermolecular* processes. Hickinbottom found [108] that when benzylphenyl ether is heated in quinoline the benzyl and phenoxy groups attack the same positions of the quinoline nucleus.

**Rearrangement of Phenolic Esters (Fries Rearrangement).** When phenyl esters are heated with aluminium chloride, zinc chloride

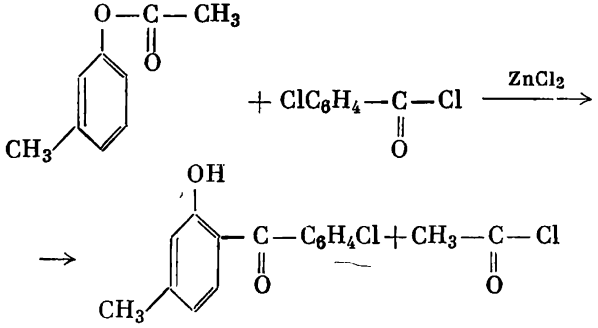
* For the stereospecific features of the rearrangement see review [104].

and ferric chloride, *o*- or *p*-oxyketones are formed, for example:

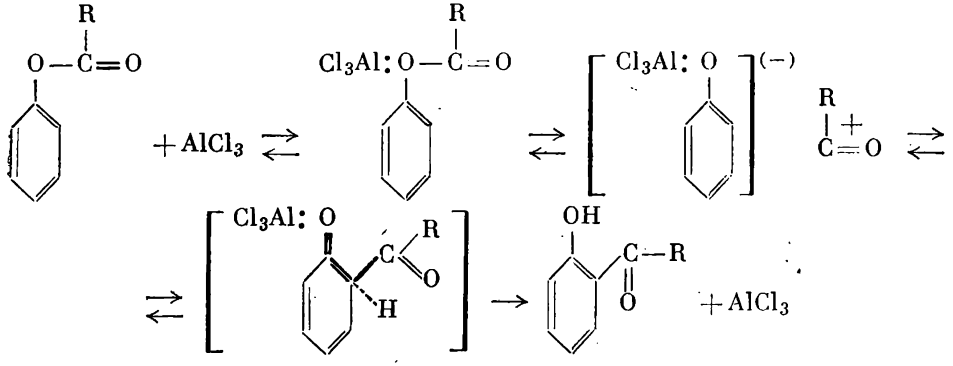


This rearrangement is called the Fries rearrangement. Fries, Auwers and coworkers studied many examples of reactions of this type and considered the Fries rearrangement to be *intramolecular* [109].

However, there is evidence that the acyl group becomes free in the course of the rearrangement. Thus, heating a mixture of *m*-tolyl acetate and *m*-chlorobenzoyl chloride with zinc chloride leads to the formation of benzophenone derivatives [110], or the acetyl group is exchanged for chlorobenzoyl:



Of the *intermolecular* mechanisms suggested to account for the Fries rearrangement, the one deserving the most attention is that according to which the ester reacts with aluminium chloride initially to form an adduct which later produces an acyl cation. The latter acylates the nucleus in the *o*- or *p*-position [111]:



Substitution of the acyl group into the nucleus is an ordinary electrophilic reaction. This is confirmed by the fact that orientants

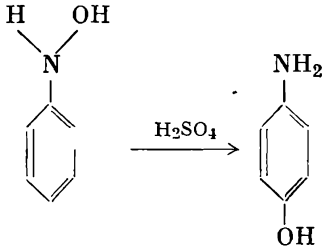
of the 1st kind facilitate the reaction. Thus if the *o*-positions in the phenyl ethers are activated by strong electron-donor groups the rearrangement can take place even at low temperatures.

### 9-2.2 Nucleophilic Rearrangements in the Aromatic Series

Aromatic nucleophilic (anionotropic) rearrangements are rearrangements, in the course of which the migrating group is transferred from the side chain into the aromatic nucleus as a nucleophilic particle with an electron pair, by means of which it was linked to the side chain.

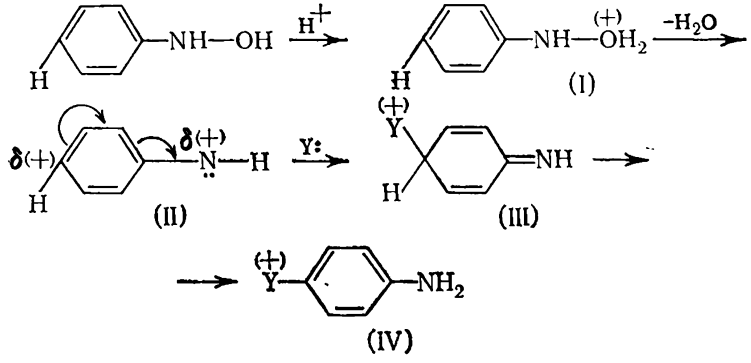
The rearrangement of hydroxylamines may serve as an important example of *intermolecular* rearrangements of this type.

**Hydroxylamine Rearrangement.** *p*-Aminophenol is formed when phenylhydroxylamine is treated with dilute sulphuric acid:




This rearrangement was discovered and studied extensively by Bamberger [112].

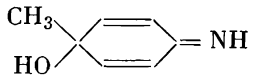
According to the current point of view [113] the hydroxylamine rearrangement is a nucleophilic *intermolecular* reaction. In the first stage of the reaction a proton adds to hydroxylamine forming an oxonium ion (I). The latter loses water and is transformed into cation (II) with a partial positive charge on the carbon atom in its *p*-position. Cation (II) reacts further with a molecule of a nucleophilic reagent Y; generally an unstable compound (III) results, from which an isomeric end product (IV) is formed by transfer of a proton from the *p*-carbon atom to the nitrogen atom:



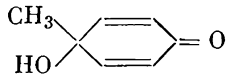
Experimental evidence is in agreement with the above reaction mechanism. Thus, a number of facts confirm that the *para*-position of cation (II) may be attacked not only by the eliminated water molecule, but also by other nucleophilic agents present in the reaction mixture. In the rearrangement of phenylhydroxylamine under the influence of aqueous sulphuric acid *p*-aminophenol is the principal product. However, if methanol is added, *o*- and *p*-anisidines are formed as by-products; if ethanol is added, *o*- and *p*-phenetidines are formed as by-products. In rearrangements catalyzed by hydrochloric acid the by-products are *o*- and *p*-chloroanilines. In the presence of phenol *p*, *p'*-$HOC_6H_4-C_6H_4-NH_2$ and $C_6H_5NH-C_6H_4-OH(p)$ are observed to form, and in the presence of aniline $-C_6H_5-NH-C_6H_4NH_2(p)$.

The appearance in the end product of groups other than hydroxyl indicates that the rearrangement is intermolecular. Since the source of these groups are the nucleophilic molecules (and anions)—methanol, ethanol, chloride anion, phenol, aniline—it must be assumed that in the course of the rearrangement an electrophilic intermediate compound (cation II) is formed, which reacts with the nucleophilic molecules.

In several cases Bamberger succeeded in establishing the formation of an intermediate product of type (III). Thus, after the rearrangement of *p*-tolylhydroxylamine in aqueous acids at a low temperature he succeeded in isolating iminoquinol (V) and quinol (VI):




(V)



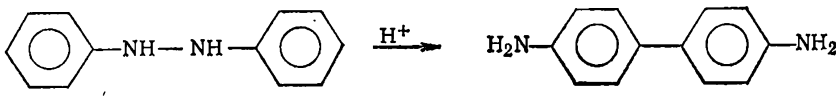

(VI)

In these cases formation of the end reaction product (of type IV) by prototropic transformation is impossible, because hydrogen is replaced by a methyl group.

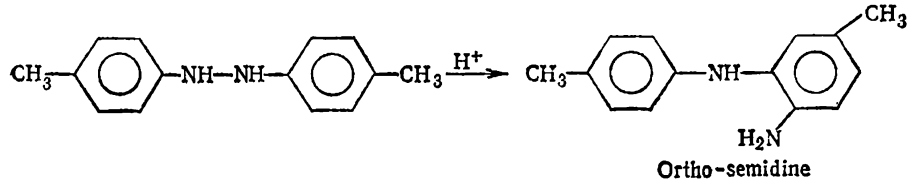
### 9-2.3 Aromatic Intramolecular Rearrangements

The four most important intramolecular aromatic rearrangements will be considered here, viz.: benzidine rearrangement, nitroamine rearrangement, rearrangement of sulphamic acids and the rearrangement of benzyltrialkylammonium and benzyldialkylsulphonium salts.

**Benzidine Rearrangement.** Hydrazobenzene changes into benzidine (4,4'-diaminobiphenyl) under the action of acids:

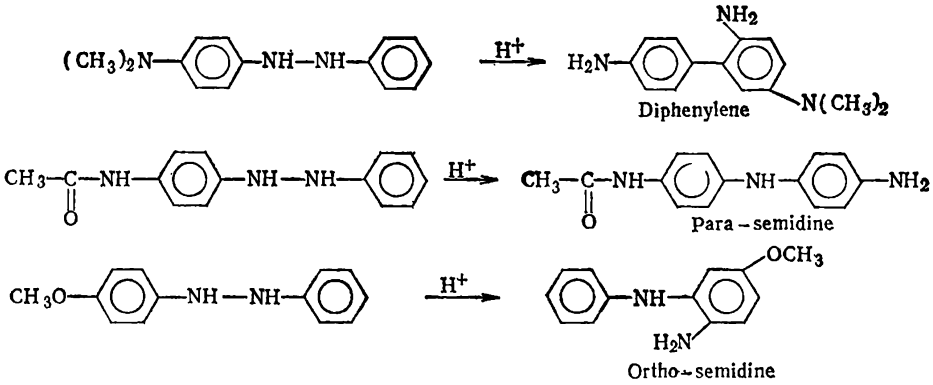


When both positions in the molecule of the initial hydrazobenzene are occupied by substituents, *ortho*-semidine usually results, e.g:




Ortho-semidine

If only one *para*-position of the initial hydrazobenzene molecule is substituted, 2,4′-diaminobiphenyl derivatives (diphenylenes), *para*-semidines, *ortho*-semidines or a mixture of these substances may form:

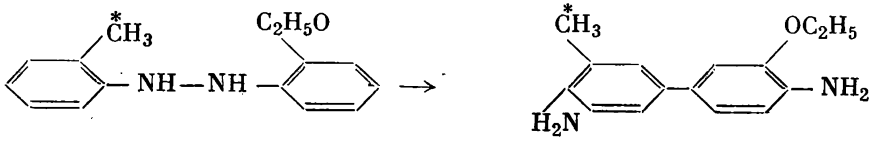



The first explanations of benzidine rearrangement were based on the supposition that the nitrogen-nitrogen bond is broken first forming two free radicals [114] or ions [115]. The interaction of the latter results in benzidine.

At present, however, it has been established definitely that the rearrangement is *intramolecular* in nature and that no molecular fragments (radicals or ions) of hydrazobenzene exist in the course of it as kinetically independent particles.

The absence of free radicals in the course of the rearrangement was proved [116] by studying the benzidine rearrangement of 2-methyl-2′-ethoxyhydrazobenzene, containing a labeled carbon atom in its methyl group. After effecting the rearrangement of this substance, ordinary 3,3′-dimethylbenzidine (*o*-tolidine) was first added and then removed from the reaction mixture. It was not labeled and, therefore, in the course of the rearrangement of 2-methyl-2′-ethoxyhydrazo-

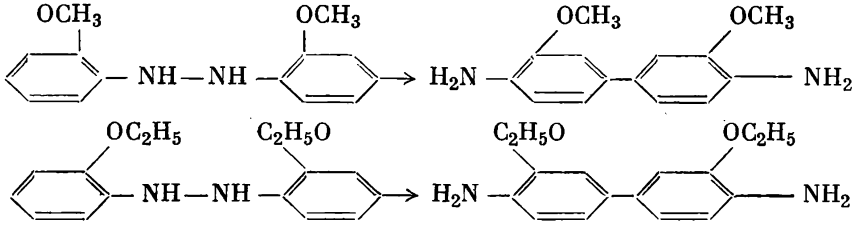
benzene



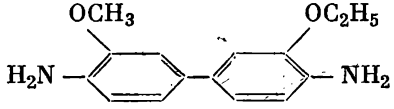
no free $o\text{-}\overset{*}{C}H_3C_6H_4\dot{N}H$ radicals are formed, as they could have reacted with each other to give radioactive *o*-tolidine.

A study of the rearrangement of 2,2′-dimethoxyhydrazobenzene and 2,2′-diethoxyhydrazobenzene [117] shows that no free ions are formed during the benzidine rearrangement.

Each of these substances undergoes rearrangement in mixture independently of the other substance; as a result only two reaction products are formed:



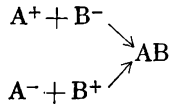
If the migrating groups (ions) were free for any length of time, a third substance should have also formed:



because, if the first two substances were formed through heterolytic reactions of two symmetrical molecules:

$$A^+ + A^- \longrightarrow AA$$
$$B^+ + B^- \longrightarrow BB$$

then there should be no hindrance to the formation of a third substance via the same heterolytic reaction:

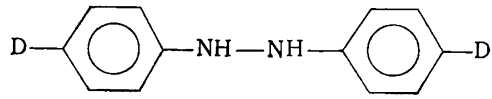


The benzidine rearrangement is a reaction of the third order. Its rate is proportional to the concentration of hydrazobenzene and to the square of the hydrogen-ion concentration [118].

$$v = \alpha[\mathrm{PhNHNHPh}]\,[H^+]^2$$

Evidently, a double cation $Ar - \overset{+}{N}H_2 - \overset{+}{N}H_2 - Ar$ takes part in the slow stage of the reaction determining the rate of the rearrangement.

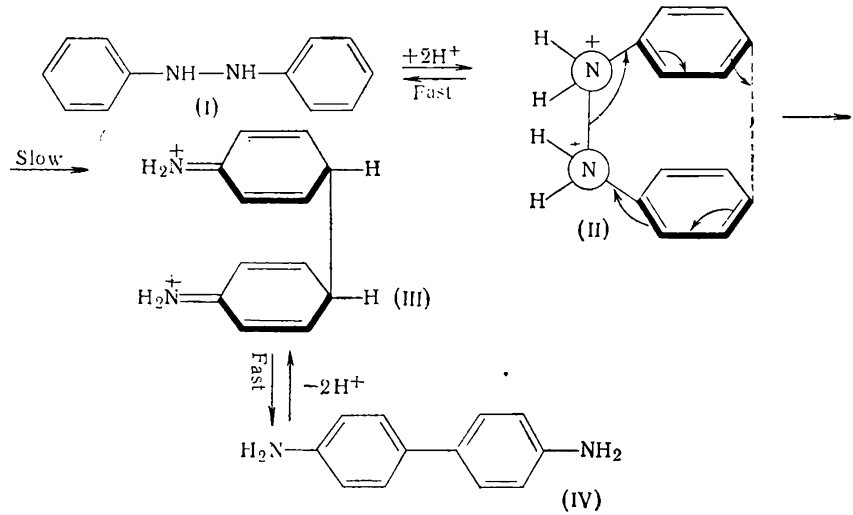
It was also found that *para*-deuterated hydrazobenzene




undergoes benzidine rearrangement practically at the same rate as the undeuterated hydrazobenzene [119].

Consequently, the *para*-hydrogen atoms, evidently, do not separate during the slowest stage of the rearrangement, but do so later.

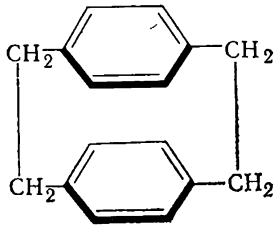
Available experimental evidence concerning the benzidine rearrangement suggests the following mechanism:




After the addition of two protons to hydrazobenzene (I) the link between the singly charged nitrogen atoms in the resulting cation (II) starts to break in such a way that the electron pair is shifted toward one of the nitrogen atoms; a new bond begins to form between the *para*-positions of the benzene nuclei. As a result of this slow stage of rearrangement an unstable intermediate compound (III) is formed, in which the *para*-carbon atoms of the benzene rings are linked by a covalent bond. Finally two protons are eliminated (fast stage) resulting in benzidine (IV).

It should be noted, however, that currently we are still unable to answer two important questions concerning the mechanism of benzidine rearrangement.

In the first place it is not clear what forces hold the two benzene rings in the activated complex so close to each other in a parallel position. Approach of two parallel benzene rings to a distance less than 3.7 Å should be greatly impeded because of the repulsion of their π electrons. The di-*p*-xylylene molecule may be used to confirm this [120].

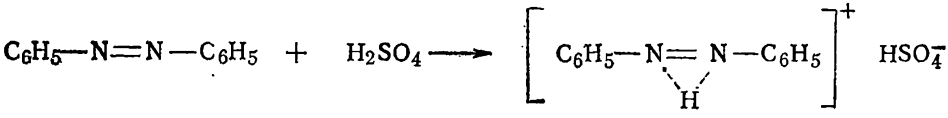


The benzene rings in this molecule are distorted, probably due to the interference of the contracted π-electron clouds.

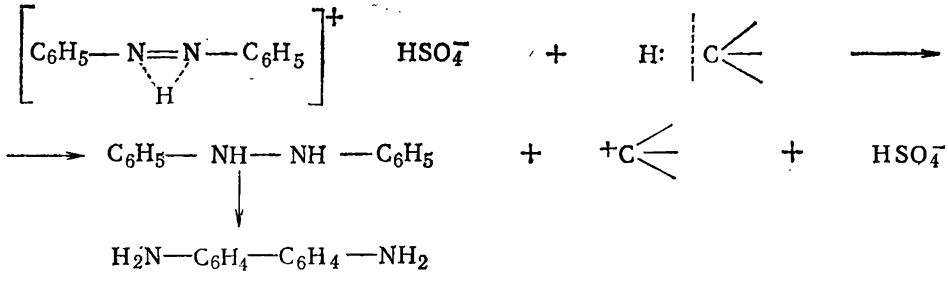
The second unsolved question relates to the influence of *para*-substituents in monosubstituted hydrazobenzenes upon the nature of the rearrangement. It is unclear, for example, why *p*-Cl favours the formation of biphenylene, *p*-$CH_3$ the formation of *ortho*-semidine, and *p*-$NH_2$ the formation of *para*-semidine.

Nesmeyanov and coworkers [121] discovered that benzidine results when azobenzene reacts with an acid or various hydrogen-containing organic compounds.

In the first step of the reaction a protonated azobenzene is formed [122], which is a good acceptor of hydride ions.



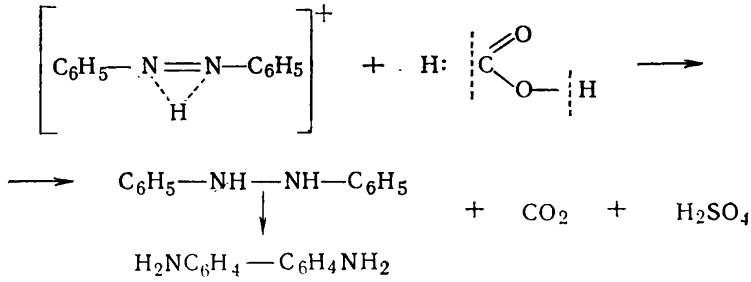
Addition of a hydride ion converts it into hydrazobenzene, which in the presence of an acid rearranges to benzidine.



The authors found that protonated azobenzene is capable of abstracting a hydride ion from a great variety of organic substances

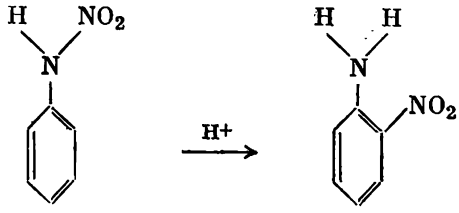
of different classes, itself being converted into benzidine. In many cases these hydride transfer reactions could be traced only by the formation of benzidine. The other reaction products were unstable carbonium ions in the majority of cases. Later they underwent a series of more or less complex transformations, resulting in the formation of stable substances. In particular, carbonium ions are often stabilized by eliminating a proton, and changing into compounds with multiple bonds. The latter polymerize in the presence of sulphuric acid forming tar-like products which have not been investigated. Hydride shifts have been established this way in reactions with acetone, cyclohexanone, acetic acid, succinic acid, benzaldehyde, dibutyl ether, benzene, thiophene, nitrobenzene, cyclohexane and *n*-hexane.

However, in a number of cases the authors succeeded in identifying both reaction products. Thus, in the reaction of protonated azobenzene with formic acid, carbonic acid was formed besides benzidine:



In the reaction with cycloheptatriene, besides benzidine a good yield of tropylium salt was formed. When benzyl alcohol was used as the hydride donor, benzaldehyde resulted.

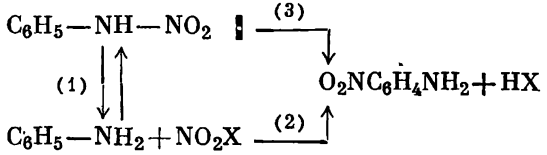
**Rearrangement of Nitroamines.** Nitroamines, which may be obtained by treating amines with nitric acid in acetic anhydride, rearrange under the influence of acids to *o*-nitroanilines or their derivatives, [123], e.g.:



A small amount of *p*-isomers sometimes forms as a by-product. The nitro group is even capable of displacing other groups and atoms (for example, bromine) if they are in the *o*- and *p*-positions.

Three hypotheses have been put forward concerning the mechanism of this rearrangement. Acc ording to one, the nitroamine rearran-

gement, like that of chloroamines, is an intermolecular two-stage process: first acidolysis of the nitro group takes place, resulting in the nitrating agent $NO_2X$ and a free amine (reaction 1) and then the amine is nitrated by the nitrating agent (reaction 2):




The second hypothesis describes the rearrangement of nitroamines as an intramolecular process (reaction 3). And finally, according to the third hypothesis, *all three reactions—the intramolecular reaction* (3) *and the intermolecular process (reactions 1 and 2)—proceed simultaneously and independently of each other.*

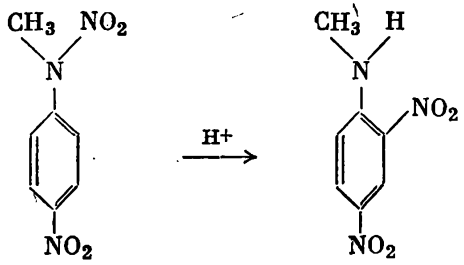
The first assumption is at odds with the facts, because the ratios of *o*-, *m*-, and *p*-isomers formed in the rearrangement of N-nitroaniline, on one hand, and in the direct nitration of aniline, on the other, are very different [124].

The rearrangement cannot be considered exclusively intramolecular because cases are known of the nitro group migrating into the nucleus of another molecule.

However, unlike chloroamines, where the presence of chlorine in the reaction mixture during the rearrangement can always be proved, formation of the nitrating agent in the rearrangement of nitroamines is generally not observed [125].

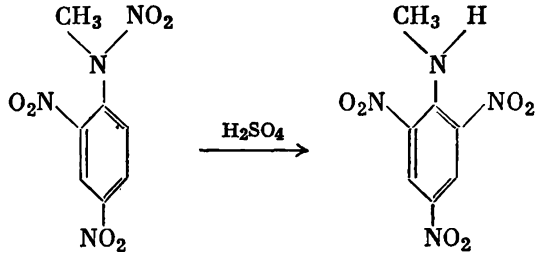
All these data may be correlated with the third hypothesis; this hypothesis also received some confirmation in a study of the rearrangement of *p*-nitrophenyl-*N*-methylnitroamine and 2,4-dinitrophenyl-*N*-methylnitroamine [126].

In the rearrangement of *p*-nitrophenyl-*N*-methylnitroamine, which proceeds under a great variety of conditions to form 2,4-dinitro-*N*-methylaniline:




there was not a single case (even in the presence of easily nitratable substances) when denitration was observed, i.e., where the formation of *N*-methyl-*p*-nitroaniline was accompanied by nitration of some other component.

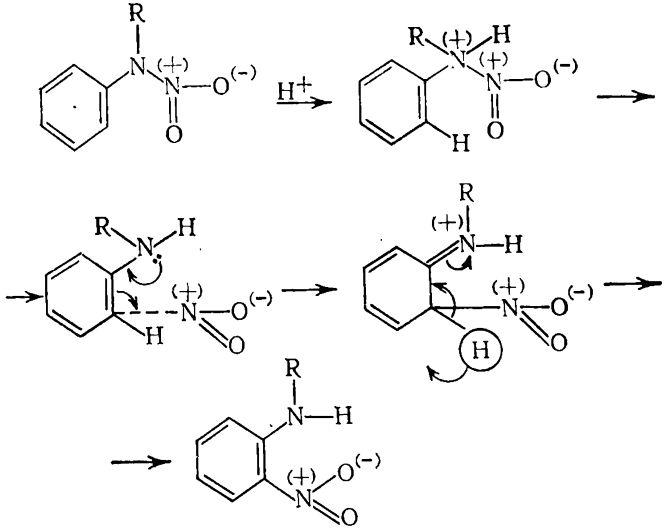
On the other hand, when 2,4-dinitrophenyl-*N*-methylnitroamine is rearranged to *N*-methyl-2,4,6-trinitroaniline




in the presence of easily nitratable substances (phenol, dimethylaniline) the nitration products of these materials are found as by-products of the rearrangement together with 2,4-dinitro-*N*-methylaniline, the product of denitration of the starting material. However, in this case neither the nitrating agent formed nor the nitric acid added are able to nitrate 2,4-dinitro-*N*-methylaniline to 2,4,6-trinitro-*N*-methylaniline (the rearrangement product) under conditions favouring the rearrangement.

In the case of *p*-nitrophenyl-*N*-methylnitroamine the rearrangement follows reaction (3) rather than reactions (1) and (2), because reaction (1) is too slow a process. In the case of 2,4-dinitrophenyl-*N*-methylnitroamine the rearrangement also proceeds in direction (3) and not (1) and (2), because although reaction (1) takes place, reaction (2) is too slow; instead of it nitration of other easily nitratable compounds present in the reaction mixture takes place.

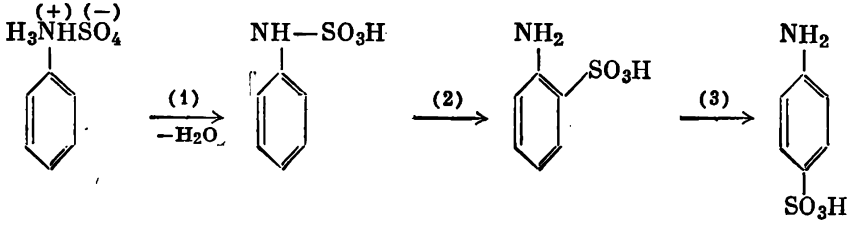
The mechanism of the rearrangement, taking into account only the intramolecular reaction (3), may be represented by the following diagram:



**Rearrangement of *N*-Sulphamic Acids.** Sulphamic acids can be prepared from amines by two methods. According to one of them the amine, say aniline, is heated with oleum at a high temperature. As the sulphonation reaction is reversible, the importance of the thermodynamic factor is paramount. Independently of the reaction mechanism (whether it is direct sulphonation of amine sulphate in the nucleus or sulphonation through the stage of formation of an *N*-sulpho acid followed by the rearrangement) the thermodynamically more stable reaction product—sulphanilic acid—is formed.

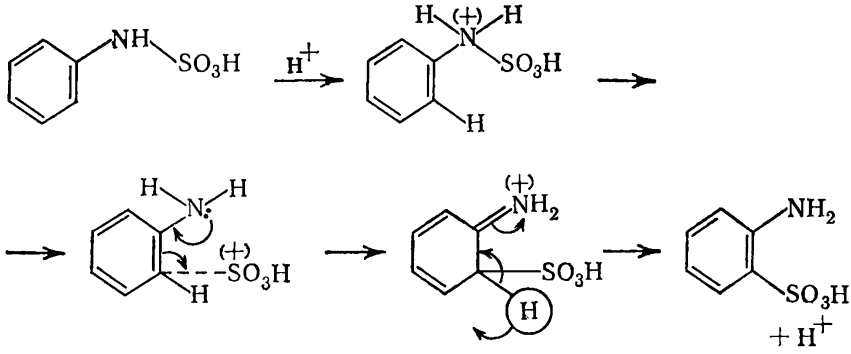
The second method of preparing aminosulpho acids consists in moderate heating of previously obtained amine sulphate (known as the "baking process").

According to Bamberger [127] the reaction passes through the following stages:




Bamberger reproduced separately all the stages of the mechanism he proposed, except for stage (1). He also showed that the rearrangement of *N*-sulphoaniline to the *ortho*-aminosulpho acid in the presence of sulphuric acid proceeds under conditions at which aniline is not sulphonated. This fact indicates that the *ortho*-rearrangement is an *intramolecular* process.

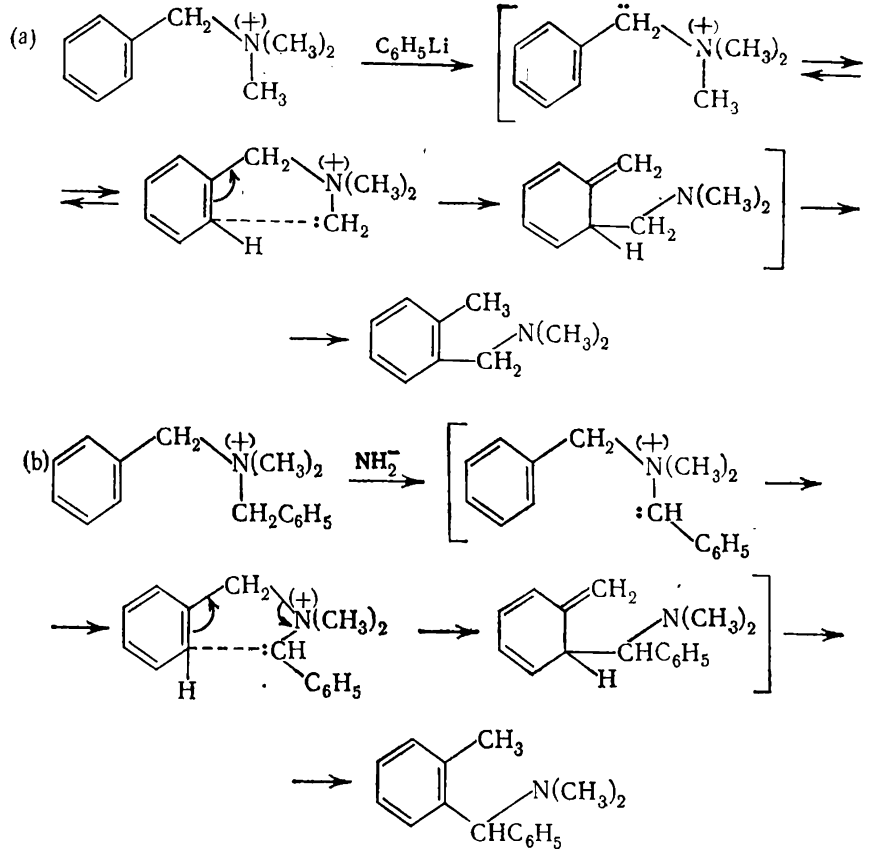
The mechanism of the *ortho*-rearrangement may be represented by a scheme analogous to that for the mechanism of nitroamine rearrangement:

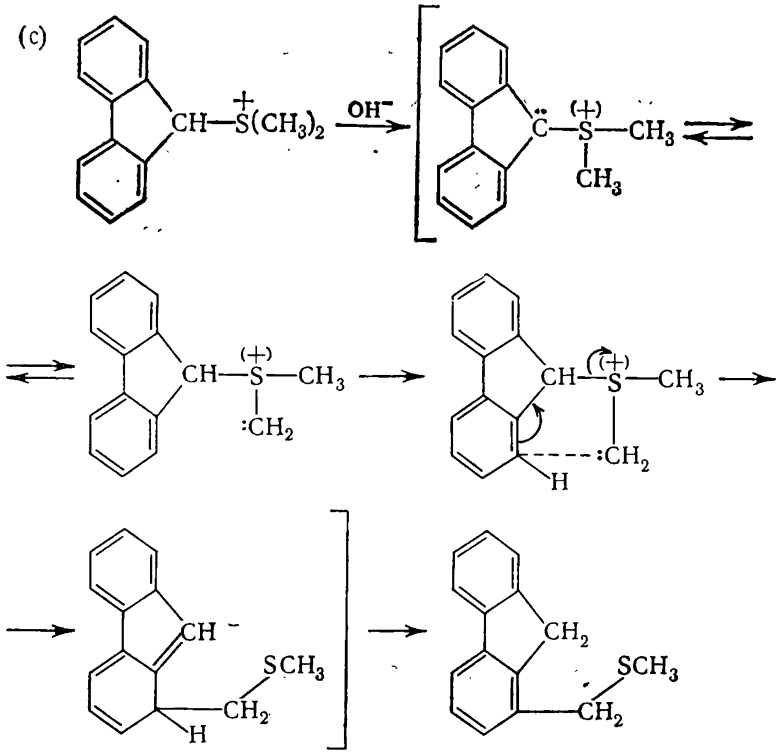


Unlike the "baking process", the high temperature sulphonation of amines with oleum is evidently largely direct sulphonation into the nucleus of the ammonium cation $ArN^+H_3$. This follows, for instance, from the fact that in the high-temperature sulphonation of aniline and dimethylaniline by oleum much larger quantities of *meta*-isomers are formed than in the "baking process".

**Sommelet Rearrangement.** Under the action of strong nucleophilic reagents benzyltrialkylammonium or benzyldialkylsulphonium compounds undergo a rearrangement, first observed by Sommelet [128], in the course of which the trialkylammonium or dialkylsulphonium group adds to the *ortho*-carbon atom of the benzene ring through an α-carbon atom of one of the alkyl groups.

Three examples of the Sommelet rearrangement are given below: (*a*) rearrangement of benzyltrimethylammonium salts [129]; (*b*) rearrangement of dibenzyldimethylammonium salts [130], and (*c*) rearrangement of 9-fluorenyldimethylsulphonium salts [131]. The intermediate reaction products are shown in brackets:





The Sommelet rearrangement resembles the Stevens rearrangement (page 586); there are proofs that both rearrangements may proceed simultaneously.

The Sommelet rearrangement is an *intramolecular* process because the migrating group is incapable of entering the nuclei of other molecules.

### 9-2.4 Rearrangements of Free Radicals

**Rearrangement of Free Radicals in the Gas Phase.** The first data on the possibility of isomerization of free alkyl radicals was published in 1936 by Glazebrook and Pearson [132]. While studying the photolysis of diisopropyl ketone to obtain free isopropyl radicals the authors discovered that the free radicals reacting with the metallic tellurium and lead mirrors and identified as mercury derivatives formed *n*-propyl instead of isopropyl mercury derivatives. This led to the hypothesis that the initially formed isopropyl radicals isomerize into *n*-propyl radicals:

$$CH_3—\dot{C}H—CH_3 \longrightarrow CH_3—CH_2—CH_2.$$

However, this hypothesis has not been proved as yet, because the free radical nature of the reaction has not been proved (it is possible that the reaction of the propyl radicals with mercury is a surface reaction).

In the absence of mercury this isomerization is not observed.

Semenov considered the question of isomerization as a general property of free radicals [133].

The only difference between substitution reactions and isomerization reactions is that in the former the radical tears an atom away from another molecule, whereas in the latter an atom is transferred intramolecularly within the radical.

Kinetically isomerization differs from substitution in the two following features:

(1) Isomerization is a monomolecular process, whereas substitution is a bimolecular process.

The rate of isomerization is given by the expression:

$$v_{isom} = 10^{13} e^{E_1/RT} (R),$$

and that of substitution, by the expression

$$v_{subst} = 10^{-10} e^{-E_2/RT} (R)(M),$$

$(R)$ being the concentration of radicals and $(M)$, the concentration of molecules. At atmospheric pressure where $(M) \simeq 10^{19}$ the ratio $v_{isom}/v_{subst}$ equals:

$$v_{isom}/v_{subst} = 10^4 e^{-\frac{E_1 - E_2}{RT}}$$

(2) Since the "attack on the bond" by the free valence in isomerization takes place at an angle which does not equal zero, evidently, $E_1 - E_2 = \Delta E > 0$.

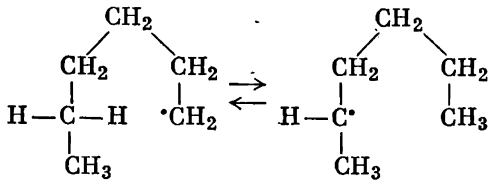
At high temperatures (when the factor $e^{-\Delta E/RT}$ is small) isomerization should prevail over substitution. At low temperatures the bimolecular substitution reaction will prevail.

During the last two decades a number of "cracking" reactions, hydrocarbon oxidations, polymerizations, etc., were studied, which cannot be accounted for without introducing the hypothesis that free radicals undergo isomerization.

Of the studies where isomerization of radicals formed in the course of reactions is assumed, and in which isomerization evidently does actually take place, the following deserve attention.

Investigating the thermal cracking of hydrocarbons, Kostyakoff and Rice [134] came to the conclusion in 1944 that isomerization of free radicals formed during cracking is a possibility. On the basis of an analysis of the products of decomposition of hexane, heptane and octane the authors concluded that long-chain free radicals are

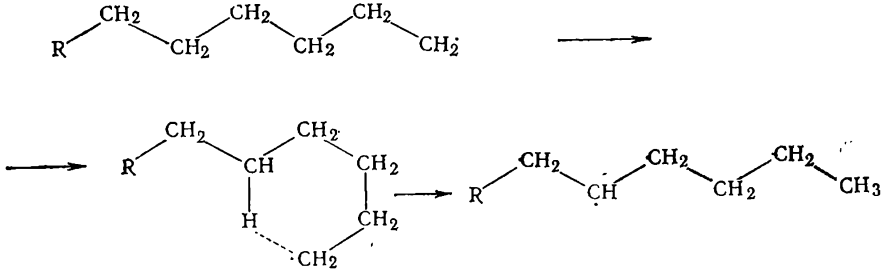
capable of intramolecular isomerization, e.g.:



In a study of the photochemical oxidation of hydrocarbons by sensitized mercury at 100°, Fok and Nalbadyan [135] came to the conclusion that the intermediate peroxide radicals isomerize

$$CH_3—O—O^{\bullet} \longrightarrow {}^{\bullet}CH_2—O—O—H$$

Studying the free radical polymerization of ethylene, Roedel [136] established two types of chain branching depending on the conditions of polymerization. He assumed that short chain branching develops during the intramolecular transfer of hydrogen through the cyclic intermediate state:



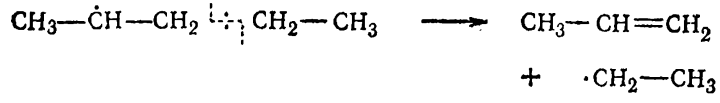
Voyevodsky and Mardaleishvili [137] assume that the alkyl free radicals formed during the reaction of addition of hydrogen atoms to alkenes isomerize in the gas phase.

Gordon and McNesby [138] suggest that free radicals isomerize in the reaction of ethylene (at 300-500°) with methyl radicals obtained by photolysis or acetone pyrolysis.

After establishing that the major product of the reaction is propylene (yield ~50%), they proposed the following mechanism of its formation: the reaction of the methyl radical with ethylene results in *n*-propyl and then in *n*-amyl radicals. The latter isomerize according to the scheme:

$$CH_3—(CH_2)_3—CH_2^{\bullet} \longrightarrow CH_3—\dot{C}H—(CH_2)_2—CH_3$$

and then decompose into propylene and an ethyl radical:



This mechanism was confirmed by the reaction of $\cdot CD_3$ radicals with ethylene at 300°.

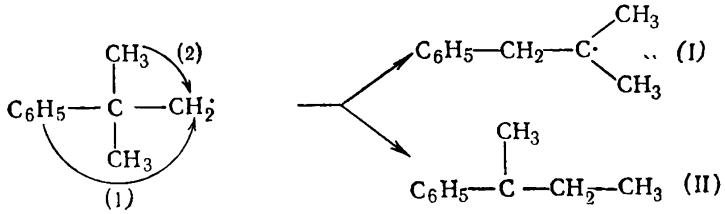
On the basis of the data obtained the authors came to the conclusion that *all higher primary n-alkyl radicals isomerize at temperatures above 250°*. This monomolecular reaction prevails over other reactions because of its relatively low energy of activation (9 kcal).

**Rearrangement of Free Radicals in Solution*.** The first unquestionable example of isomerization of a free radical in solution was studied by Urry and Kharasch [140]. The reaction of phenylmagnesium bromide and neophyl chloride in the presence of cobaltous chloride (when, as is known, the reaction follows a radical mechanism) results in *tert*-butylbenzene, isobutylbenzene, isobutenylbenzene, β,β-dimethylstyrene, and products of radical dimerization:

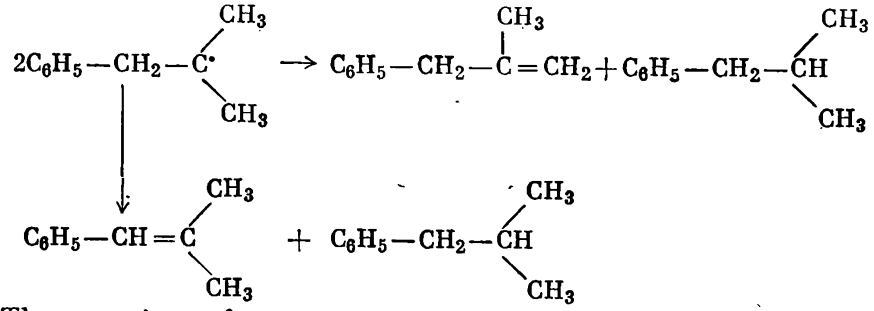
$$C_6H_5MgBr + CoCl_2 \longrightarrow C_6H_5CoCl + MgClBr$$

$$C_6H_5CoCl \longrightarrow C_6H^{\bullet} + {}^{\bullet}CoCl$$

$$C_6H_5-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2-Cl + {}^{\bullet}CoCl \longrightarrow C_6H_5-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2^{\bullet} + CoCl_2$$



The formation of the end products can be easily conceived as the result of the usual reactions of disproportionation of radicals (I) and (II) formed on rearrangement of the neophyl radical:



The reaction of organomagnesium compounds with cobaltous chloride was utilized subsequently also for studying rearrangements of free radicals.

* See [139] for review.

To establish the possibility of rearrangement of the 2-phenylpropyl and 2-phenylethyl-1-$C^{14}$ radicals Smith and Adamson [141] studied the reaction of 2-phenyl-1-bromopropane and 2-phenyl-1-bromoethane-1-$C^{14}$ with magnesium and cobaltous bromide in boiling ether.

The authors found that the 2-phenylpropyl radical formed in the reaction between 1-bromo-2-phenylpropane, magnesium and cobaltous bromide, undergoes 1,2-phenyl rearrangement (40%) yielding *n*-propylbenzene, β-methylstyrene and allylbenzene.

$$\mathrm{Ph{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}CH_2{-}Br} \xrightarrow[CoBr]{Mg}$$

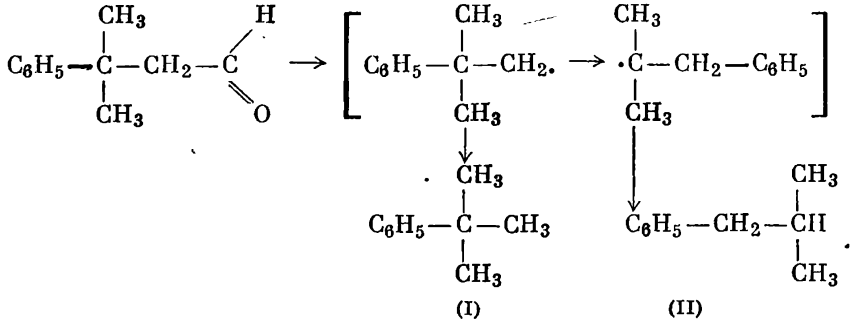
$$\longrightarrow \mathrm{Ph{-}CH_2{-}CH_2{-}CH_3 + Ph{-}CH{=}CH{-}CH_3 + Ph{-}CH_2{-}CH{=}CH_2}$$

The 2-phenylethyl-1-$C^{14}$ radical formed in a similar reaction from 2-phenylbromoethane-1-$C^{14}$ rearranged (20%) to a 2-phenylethyl-2-$C^{14}$ radical:

$$\mathrm{Ph{-}CH_2{-}\overset{*}{C}H_2{\cdot}} \longrightarrow \mathrm{{\cdot}CH_2{-}\overset{*}{C}H_2{-}Ph}$$

The most distinct results in elucidating the possibility and the nature of radical rearrangements in solution were obtained in studying the decarbonylation of aldehydes, initiated by peroxides.

In 1947 Winstein and Seubold [142] studied the decarbonylation of β-phenylisovaleraldehyde, initiated by di-*tert*-butyl peroxide. Among the reaction products the authors isolated a 1 : 1 mixture of phenyl-*tert*-butylbenzene (I) and phenylisobutylbenzene (II), which formed as a result of rearrangement of the intermediate free radical (phenyl migration):



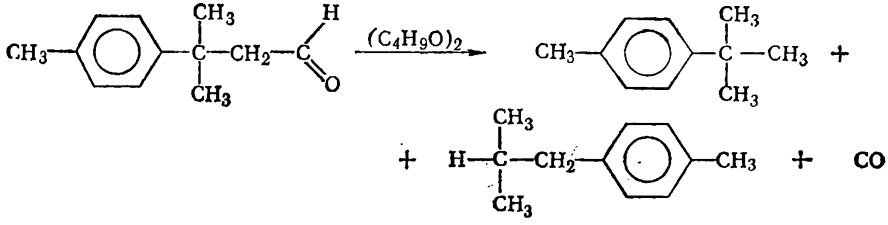
(I) (II)

Thus, the authors confirmed the rearrangement of the neophyl radical (phenyl migration) described previously by Urry and Kharasch [143].

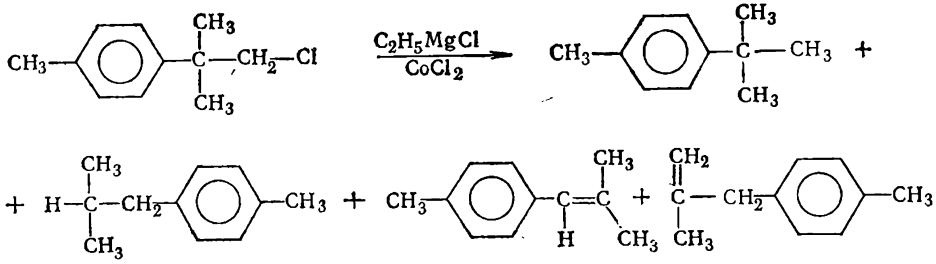
Later, in 1953, Seubold [144] studied in detail the above reaction in chlorobenzene and confirmed the 1,2-migration of the phenyl group and also established that the ratios of hydrocarbons in this reaction depend on the concentration of aldehyde; at high concentrations only phenyl-*tert*-butylbenzene (I) is formed; at low aldehyde

concentrations phenylisobutylbenzene (II) forms as well (as a result of rearrangement of the radical). Like in the previous investigations the author did not detect migration of any methyl group in the neophyl radical.

An interesting rearrangement of the free *n*-methylneophyl radical takes place during decarbonylation of β-*n*-tolylisovaleraldehyde

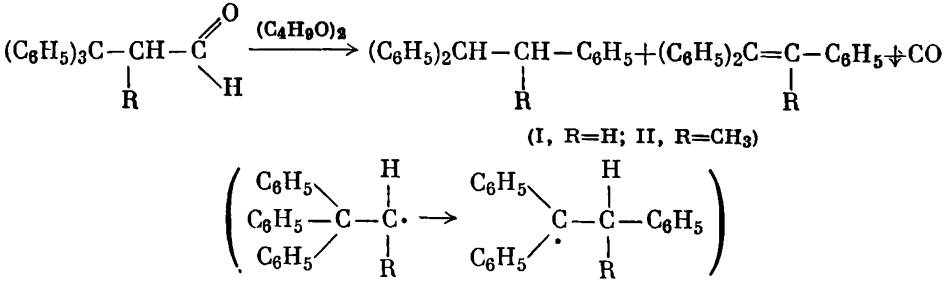


and in the reaction of ethylmagnesium bromide with *p*-methylneophyl chloride in the presence of cobaltous chloride [145].

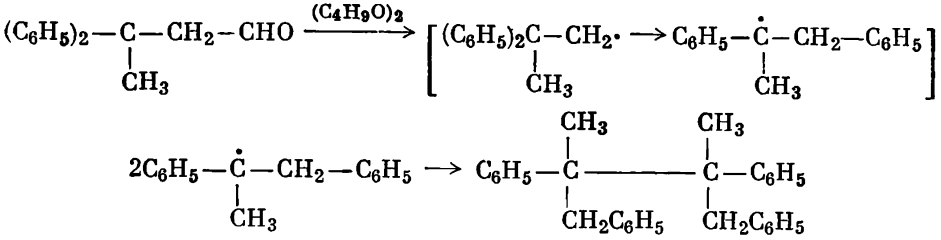


It was established that when formed in the reactions indicated above, the *p*-methylneophyl radical suffered rearrangement only through migration of the aryl group. The percentage rearrangement (50%) was the same as in the case of the neophyl radical.

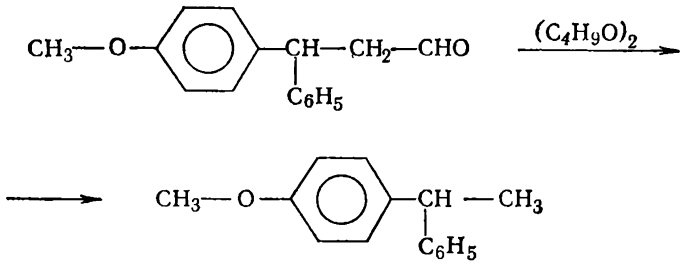
To investigate the effect of aldehyde structure upon the degree of rearrangement Curtin and Hurwitz [146[ studied the decarbonylation of four aldehydes. They found that the free radicals formed during the decarbonylation of β,β,β-triphenylpropionaldehyde (I) and α-methyl-β,β,β-triphenylpropionaldehyde (II) undergo 100% rearrangement through 1,2-migration of the phenyl.



During the decarbonylation of β, β-diphenylbutyraldehyde the free radical $(C_6H_5)_2C(CH_3)-CH_2^{\cdot}$ also rearranges through 1,2-migration of phenyl (100%) and the rearranging radical dimerizes

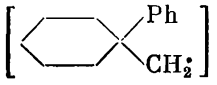


On the contrary, β-*p*-anisyl-β-phenylpropionaldehyde forms α-*p*-anisyl-α-phenylethane with retention of the carbon skeleton.

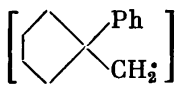


Kauer [147] established that during the decarbonylation of β-*p*-nitrophenyl-β, β-diphenylpropionaldehyde a rearrangement takes place involving migration of the *p*-nitrophenyl group, though to a much smaller extent than in the case of the phenyl or tolyl groups.

In 1958 Wilt and Philip [148] reported an interesting rearrangement of free radicals in solution. They investigated the influence of cycloaliphatic groups on the rearrangement of radicals similar to neophyl, during the decarbonylation of 1-phenylcyclopentylacetaldehyde and 1-phenylcyclohexylacetaldehyde at 140° and 190° without solvent, at 132° in chlorobenzene and at 160° in benzyl mercaptan. They established that the 1-phenylcyclohexylmethyl radical



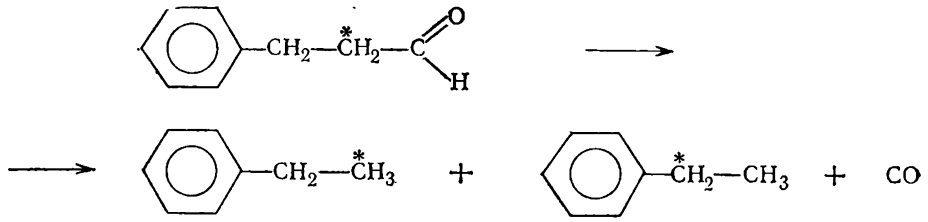
rearranges through phenyl group migration to a greater extent than the 1-phenylcyclopentylmethyl radical



The percentage rearrangement in chlorobenzene was higher than in the decomposition of aldehyde in the absence of any solvent and was practically the same for both radicals. Benzyl mercaptan lowered the percentage rearrangement.

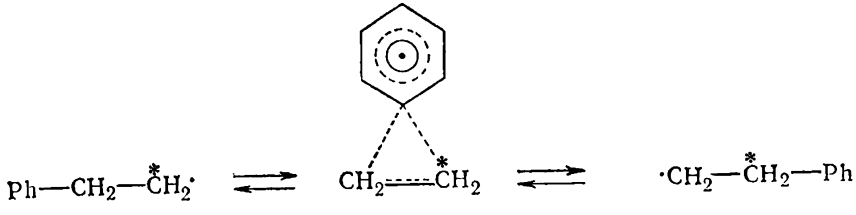
During the last few years free radical rearrangement has been studied successfully by using labeled atoms. With the aid of this method a number of new rearrangements have been discovered and the mechanisms of well-known rearrangements elucidated.

Using $C^{14}$, in 1959 Slaugh [149] discovered a 1,2-rearrangement of phenyl in the 2-phenylethyl-1-$C^{14}$ radical formed during the decarbonylation of 3-phenylpropion-2-$C^{14}$-aldehyde catalyzed by di-*t*-butyl peroxide:



Having studied the dependence of the percentage rearrangement on the temperature and on the addition of thiophenol, he found that with rising temperature (145-170°) the percentage rearrangement grows (from 3.3 to 5.1%); in the presence of thiophenol, on the contrary, the percentage rearrangement decreases.

When the decarbonylation reaction was carried out in the presence of tritium-labeled benzyl mercaptan it was found that no migration of hydrogen takes place in the 2-phenylethyl-1-$C^{14}$ radical. Slaugh suggested the following mechanism of isomerization of the phenylethyl radical.



(A)

This mechanism involves the formation of an intermediate nonclassical free radical (A).

Rearrangements of free radicals through migration of a halogen are known. Nesmeyanov, Freidlina, and Zakharkin [150] described the rearrangement of the $CCl_3 - \dot{C}H - CH_2X$ radical to $\dot{C}Cl_2 - - CHCl - CH_2X$ (X = Br, $CCl_3$), which takes place on addition

of bromotrichloromethane and hydrogen bromide to 3,3,3-trichloropropene-1 in the presence of benzoyl peroxide.

The addition of bromotrichloromethane to 3,3,3,-trichloropropene-1 in the presence of benzoyl peroxide should have resulted in $CCl_3 - CHBr - CH_2 - CCl_3$. Actually the reaction is much more complex. It results in the formation of many compounds from which the compounds I and II could be isolated

$CCl_3-CH_2-CH=CH_2$ (I) $\qquad$ $CCl_3-CH_2-CHCl-CCl_2Br$ (II)

as well as a compound of the composition $C_3H_3Cl_4Br$.

The formation of substance II can be explained by assuming that the intermediate $CCl_3 - \dot{C}H - CH_2 - CCl_3$ radical rearranges, and the reaction as a whole may be represented by the following scheme:

(a) $(C_6H_5COO)_2 \longrightarrow C_6H_5\cdot + CO_2 + C_6H_5-COO\cdot$

$C_6H_5\cdot + BrCCl_3 \longrightarrow C_6H_5Br + \cdot CCl_3$

$\cdot CCl_3 + CH_2=CH-CCl_3 \longrightarrow CCl_3-CH_2-\dot{C}H-CCl_3$

$CCl_3-CH_2-\dot{C}H-CCl_3 \longrightarrow CCl_3-CH_2-CHCl-\dot{C}Cl_2$

(Rearrangement of the radical)

(b) $CCl_3-CH_2-CHCl-\dot{C}Cl_2 + BrCCl_3 \longrightarrow$

$\longrightarrow CCl_3-CH_2-CHCl-CCl_2Br + \cdot CCl_3$

(c) $CCl_3-CH_2-CHCl-\dot{C}Cl_2 + CH_2=CH-CCl_3 \longrightarrow$

$\longrightarrow CCl_3-CH_2-CH=CCl_2 + ClCH_2-\dot{C}H-CCl_3$

$ClCH_2-\dot{C}H-CCl_3 + BrCCl_3 \longrightarrow C_3H_3Cl_4Br + \cdot CCl_3$

$2\cdot CCl_3 \longrightarrow CCl_3-CCl_3$

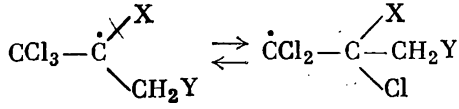
The addition of hydrogen bromide to 3,3,3-trichloropropene-1 results in a good yield of 1,1,2-trichloro-3-bromopropane, this apparently also being due to isomerization of the intermediate free radical according to the diagram:

$Br\cdot + CH_2=CH-CCl_3 \longrightarrow Br-CH_2-\dot{C}H-CCl_3$

$Br-CH_2-\dot{C}H-CCl_3 \longrightarrow Br-CH_2-CHCl-\cdot CCl_2$

$Br-CH_2-CHCl-\dot{C}Cl_2 + HBr \longrightarrow BrCH_2-CHCl-CCl_2H + \cdot Br$, etc.

Later a number of other examples were found of isomerization of radicals through a 1,2 chlorine shift [151-155].



(where X and Y=H and Cl, H and Br, H and $CCl_3$, $CH_3$ and Br, $CH_3$ and Cl, Cl and Br, Cl and Cl, Br and Br).

Skell, Allen and Gilmour [157] described a rearrangement in bromoalkyl radicals through the migration of bromine. They established that radical chain chlorination of isopropyl and *n*-propyl bromides (I) results in the same product, viz., 1-bromo-2-chloropropane, and in the case of isobutyl bromide and *tert*-butyl bromide (II), in 1-bromo-2-chloro-2-methylpropane.

$$\left.\begin{array}{l} CH_3-CH_2-CH_2-Br \\ CH_3-CHBr-CH_3 \end{array}\right\} \xrightarrow{Cl_2} CH_3-\underset{\displaystyle Cl}{\underset{|}{CH}}-CH_2-Br \qquad (I)$$

$$\left.\begin{array}{l} CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle Br}{\overset{|}{C}}}}-CH_3 \\ CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle H}{\overset{|}{C}}}}-CH_2-Br \end{array}\right\} \xrightarrow{Cl_2} CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle Cl}{\overset{|}{C}}}}-CH_2- \qquad (II)$$

In the first case it is supposed that the radical (A), formed as an intermediate during the chlorination of isopropyl bromide, isomerizes:

$$CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_3 \xrightarrow{\cdot Cl} CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_2^{\cdot}+HCl$$

$$CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_2^{\cdot} \downarrow$$

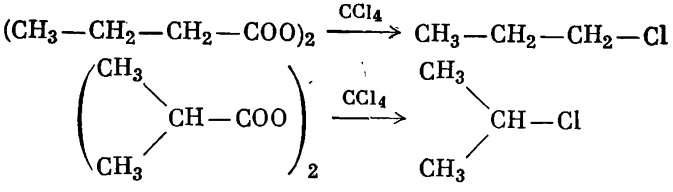
$$CH_3-\underset{\displaystyle Cl}{\underset{|}{CH}}-CH_2-Br \xleftarrow{Cl_2} CH_3-\underset{\displaystyle \cdot}{CH}-CH_2-Br \qquad (A)$$

In the second case the radical (B) formed as an intermediate in the chlorination of *tert*-butyl bromide undergoes a similar isomerization involving a bromine shift from the α-position:

$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle Br}{\overset{|}{C}}}}-CH_3 \xrightarrow{\cdot Cl} CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle Br}{\overset{|}{C}}}}-CH_2^{\cdot}+HCl \quad (B)$$

$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle Cl}{\overset{|}{C}}}}-CH_2-Br \xleftarrow{Cl_2} CH_3-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle \cdot}{C}}}-CH_2-Br$$

Until very recently it was thought that simple alkyl radicals are incapable of isomerizing in solution. This opinion was based on Kharasch's work [156], in which he established that the decomposition of *n*-butyryl peroxide in carbon tetrachloride results only in *n*-propyl chloride, and the decomposition of isobutyryl peroxide yields isopropyl chloride as the sole product.



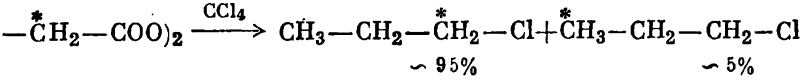
Recently DeTar studied the decomposition of δ-phenylvaleroyl peroxide and *n*-heptanoyl peroxide in carbon tetrachloride and on the basis of the nature of the reaction products came to the conclusion that the radicals

$$C_6H_5-CH_2-CH_2-CH_2-CH_2^{\bullet} \quad \text{and} \quad CH_3-CH_2-CH_2-CH_2-CH_2^{\bullet}$$

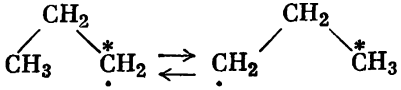
do not isomerize [158, 159].

It was also established [160] that the primary free radicals formed in the liquid-phase photochlorination of isobutane do not isomerize into tertiary radicals.

The first unquestionable case of isomerization of an alkyl radical in solution under mild conditions was found during a study of decomposition of *n*-butyryl peroxide with a $C^{14}$-labeled α-carbon atom [161].



It was shown that the *n*-propyl radical undergoes isomerization involving a hydrogen shift in the β-position:

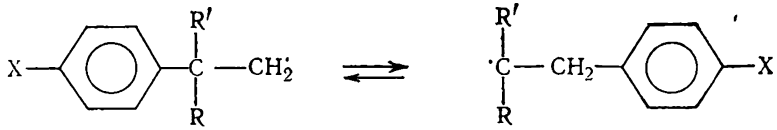


On the basis of steric considerations it is easy to come to the conclusion that a β-shift of hydrogen in a free radical is preferable to α-shift. It is because of this that Kharasch detected no α-shifts. As to β-shift in the propyl radical, he could not detect it because his peroxide was not labeled.

On the basis of available experimental data on the rearrangements of free radicals several of their characteristic features may be enumerated.

Free radicals are capable of skeletal rearrangements, and also of rearrangements due to migration of hydrogen or halogen atoms.

In the case of arylalkyl radicals rearrangements involve migration of the phenyl group from the α-position:



(R,R′ = alkyl, aryl, hydrogen)

Alkyl free radicals are capable of isomerization when migration of hydrogen from the β or from more distant positions is possible.

The percentage rearrangement increases with rising reaction temperature.

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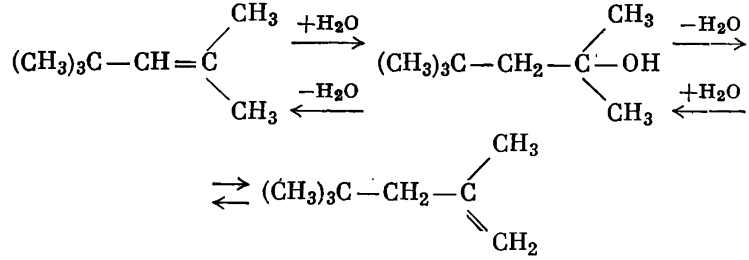
# 10

# TAUTOMERISM AND DUAL REACTIVITY

## 10-1 TAUTOMERISM

### 10-1.1 The Rise and Development of the Concept of Tautomerism

In 1877 Butlerov attributed the formation of two isomeric isobutenes in the reaction of sulphuric acid with trimethylcarbinol to dynamic isomerism:



In his paper, "Isodibutylene", Butlerov wrote [1]: "In the great majority of cases we have to do with substances which at chemical equilibrium under ordinary conditions contain infinitely greater numbers of particles of a single known definite chemical structure in their gaseous or liquid mass than particles of other structures, isomeric with the first. There are probably also cases, however, where the mass of a substance always contains perceptible amounts of isomeric particles of different chemical structures, particles forever "competing" with each other, rearranging from one structure to another. In the first case a definite chemical structure can be indicated for the substance, but in the second case it could be useless to speak of any single definite structure because the mass of the substance contains particles of different, say two, structures. Owing to the tendency of the particles to rearrange, the entire mass is subject to reactions peculiar to one structure, or peculiar to the other, depending on the kind of reagent acting on it, depending, so to speak, on the trend of the reaction."

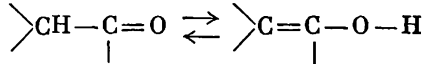
An entirely different point of view was expressed by Laar [2], who introduced the term "tautomerism" into the science of chemistry.

By "tautomerism" Laar meant the phenomenon of a substance reacting chemically according to two possible structures, i.e., essentially, dual reactivity. Laar ascribed this ability to a peculiar state—oscillation of the atoms of the tautomeric substance. Thus, according to Laar, the reason for tautomerism of hydrocyanic acid is not the existence of the discrete molecules HCN and HNC, capable of interconversion, but that the hydrogen atom keeps oscillating constantly (similar to the oscillation of double bonds in the benzene ring after Kekulé) between the nitrogen and the carbon, so that all the molecules of hydrocyanic acid have the same structure.

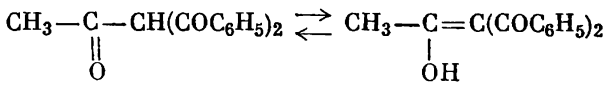
Laar's conception of the nature of tautomerism was erroneous. Science accepted Butlerov's postulation of tautomerism as equilibrium isomerism.

Proofs confirming the correctness of Butlerov's theory were obtained in 1896 in the work of Claisen, Wislicenus and Knorr [3], who separated tautomeric forms of some diketones and keto esters in the pure state and showed that they can easily be converted into an *allelotropic mixture* (equilibrium mixture of tautomers).

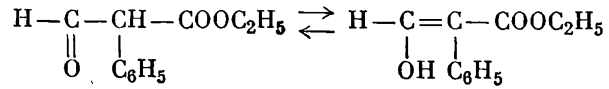
Thus, in the case of keto-enol tautomerism, which may be represented schematically as follows:



the existence of keto and enol tautomers was proved. For instance, tautomers of acetyldibenzoylmethane were obtained:

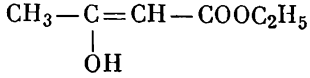


and tautomers of ethyl formylphenylacetate:

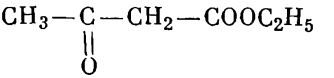


Investigations of the structure and reactivity of acetoacetic ester were of particular significance for the entire problem of tautomerism.

Heiter [3], who prepared acetoacetic ester in 1863, ascribed to it the enol form:



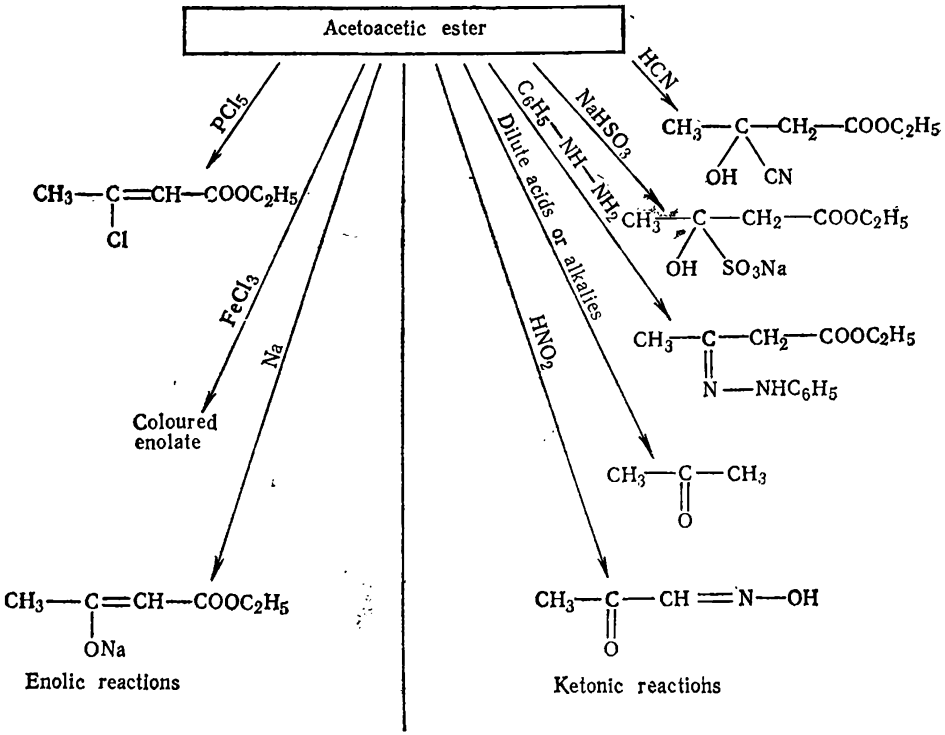
Frankland and later Wislicenus thought the keto form correct:



These differences in opinion were due to the ability of acetoacetic ester to give ketonic or enolic reactions depending on the particular reagent. Metallic derivatives of acetoacetic ester do not resemble organometallic compounds at all. There is no doubt that they are enolates, for example $CH_3 - C(ONa) = CH - COOC_2H_5$. Acetoacetic ester, like other enolates, gives a characteristic colour reaction with ferric chloride. It reacts with phosphorus pentachloride forming ethyl β-chlorocrotonate:

$$CH_3 - CCl = CH - COOC_2H_5$$

On the other hand, acetoacetic ester, like other ketones, adds hydrocyanic acid, sodium bisulphite, reacts normally with hydroxylamine and with phenylhydrazine. Under the action of dilute acids or alkalies, acetoacetic ester yields acetone, and when acted upon by nitrous acid it gives isonitrosoacetone:




The discussion as to the true structure of acetoacetic ester ended only in 1911 when Knorr [4] succeeded in isolating both tautomers in pure form.* The keto form was obtained in the crystalline state

* Cases of tautomerism, where both isomers can be isolated or detected in a mixture by analytical means, are called *desmotropy*.

by freezing the ether solution at —78°. The enol form was obtained by treating a solution of sodioacetoacetic ester in dimethyl ether with gaseous hydrogen chloride at —78°; the ester of hydroxycrotonic acid separated out as an oil:

$$CH_3-C(ONa)=CH-COOC_2H_5 \xrightarrow[-78^\circ]{HCl} CH_3-C(OH)=CH-COOC_2H_5$$

The keto form gives no colour reaction with ferric chloride and does not react with bromine. The enol form dissolves in alkali, gives a colour reaction with ferric chloride and adds bromine. Knorr succeeded in isolating the tautomers in pure form because he worked at such a low temperature, at which interconversion of tautomers is very slow. At ordinary temperatures both forms of acetoacetic acid gradually form a tautomeric equilibrium mixture consisting of 93% of the keto and 7% of the enol form.

Later Kurt Meyer [5] succeeded in separating acetoacetic ester into tautomers by the use of "asceptic" distillation. According to this method the material is subjected to fractional distillation from a quartz or Jena glass flask which underwent special treatment to guarantee the absence of impurities, because the latter catalyze tautomeric equilibrium.

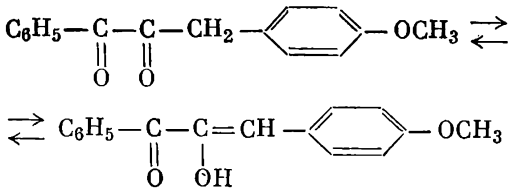
In the example of acetoacetic ester, Butlerov's explanation of tautomerism as dynamic isomerism received the most direct confirmation. Other examples of keto-enol tautomerism were found in studying α-diketones. Thus, the pure keto and enol forms of methylbenzylglyoxal, phenylbenzylglyoxal and phenyl-*p*-methoxybenzylglyoxal [6] were isolated.

$$CH_3-C(=O)-C(=O)-CH_2-C_6H_5 \rightleftarrows CH_3-C(=O)-C(OH)=CH-C_6H_5$$

Methylbenzylglyoxal

$$C_6H_5-C(=O)-C(=O)-CH_2-C_6H_5 \rightleftarrows C_6H_5-C(=O)-C(OH)=CH-C_6H_5$$

Phenylbenzylglyoxal



Phenyl-*p*-methoxybenzylglyoxal

The keto forms were obtained by distillation over an alkaline catalyst (soda), and the enols by crystallization in the presence of alkali or an organic base. These tautomeric substances are relatively stable and show no tendency to form an equilibrium mixture in the absence of catalysts.

### 10-1.2 Borderline Between Tautomerism and Isomerism

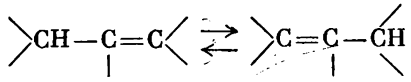
Keto-enol tautomers (for instance, those of acetoacetic ester) are stable at a sufficiently low temperature and are practically not interconvertible; at ordinary temperatures tautomeric interconversions take place readily.

Instances are known when isomeric substances which are stable under ordinary conditions are capable of interconversion at higher temperatures (often with the aid of catalysts).

Thus, isomeric vinylacetic and crotonic acids, stable under ordinary conditions, are capable of interconversion in hot alkaline solution [7]:

$$CH_2=CH-CH_2-COO^- \overset{OH^-}{\rightleftarrows} CH_3-CH=CH-COO^-$$

Like in the interconversions of diisobutylenes which occur at room temperature under the influence of sulphuric acid (page 631), in this case tricarbon tautomerism takes place at an elevated temperature:



Favorsky found [8] that propyl bromide and isopropyl bromide which are stable isomers under ordinary conditions form an equilibrium mixture at 250° (in a sealed tube):

$$CH_3-CH_2-CH_2-Br \overset{250°}{\rightleftarrows} CH_3-\underset{\displaystyle Br}{\underset{|}{CH}}-CH_3$$

From the examples cited it follows that there is no sharp borderline between isomerism and tautomerism. Substances which are isomeric under certain given conditions are tautomeric under more drastic conditions.*

---

* In this connection it should be noted that the term *dynamic isomerism* reflects the phenomenon better than the term *tautomerism*, although the latter is generally accepted.

### 10-1.3 Mechanism and Types of Tautomeric Conversions

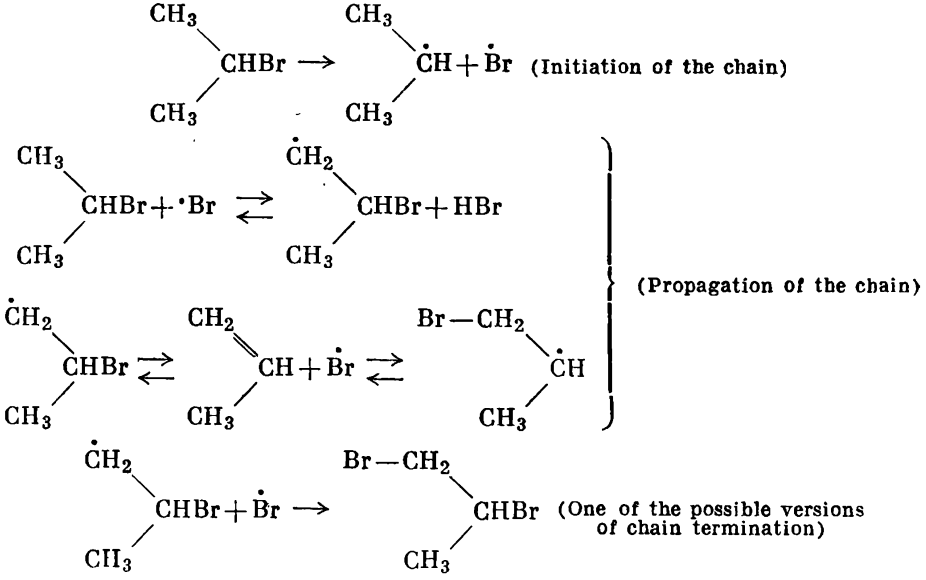
The nature of breaking and forming of chemical bonds divides reactions into homolytic and heterolytic—radical and ionic. It may be postulated that tautomeric conversions of both types must exist. However, up to the present time only heterolytic (ionic) tautomeric conversions have been studied almost exclusively.

There is every reason to believe that the tautomeric conversion of allyl bromides catalyzed by oxygen and hydrogen bromide is of a homolytic nature [9]:

$$Br^{\bullet} + R-CH=CH-CH_2-Br \rightleftarrows R-\underset{\displaystyle Br}{\underset{|}{CH}}-CH=CH_2 + Br^{\bullet}$$

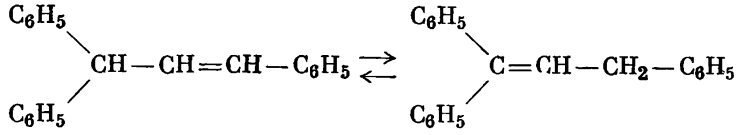
According to Favorsky, the isomerization of alkyl bromides is also, in all probability, a chain radical reversible process.

On the basis of the mechanism of thermal decomposition of propyl bromide at high temperature suggested by Semenov [10], the tautomeric conversion of isopropyl bromide into propyl bromide may be formulated as follows:

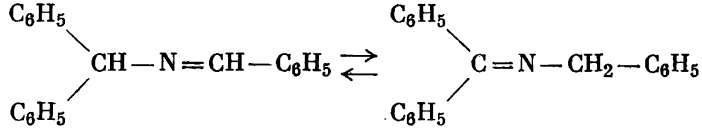



The overwhelming majority of tautomeric transformations investigated are heterolytic in nature. Tautomeric transformations, in which atoms or groups of atoms shift as cations, are called *cationotropic* tautomeric transformations. If the atoms or groups of atoms migrate as anions, the processes in which this takes place are known as *anionotropic* tautomeric transformations.

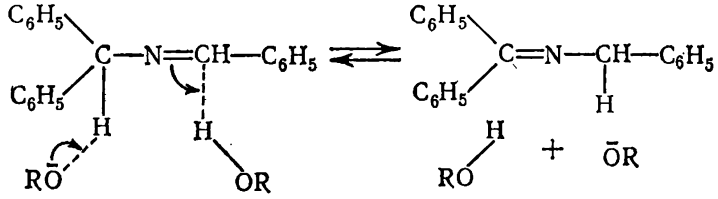
With respect to kinetic mechanism, tautomeric transformations may be subdivided into bimolecular ionizing and trimolecular. There are evidently no true monomolecular tautomeric transformations. In trimolecular processes tautomeric transformation follows a heterolytic mechanism; however, no organic ion of tautomeric material is formed in such an instance. This refers to many examples of tricarbon tautomerism, for instance, the tautomerism of triphenylpropylenes:



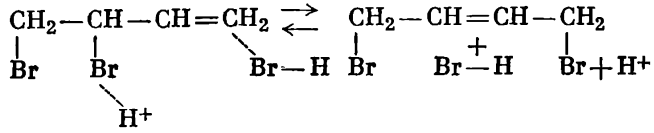
and the tautomerism of Schiff bases:



The isomers of these substances are quite stable under ordinary conditions, but under the influence of sodium alcoholate tautomerization takes place in alcoholic solution and an equilibrium is established between the two isomers. In this case the tautomeric transformation [11] is a trimolecular process—it takes place under simultaneous attack of the substance by the alcoholate anion and an alcohol molecule:

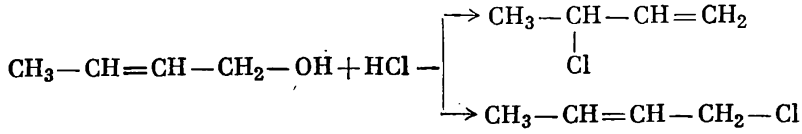


The anionotropic tautomeric conversion of 1,2- and 1,4-dibromobutenes is also a trimolecular reaction:



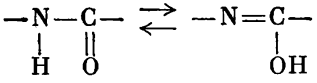
It should be pointed out that very few examples of true anionotropic tautomerism are known to date. In most cases,

probably, the allylic system shows dual reactivity, for example:

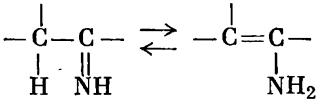


The most prevalent and well investigated cationotropic tautomeric transformations are those in which the proton migrates. They are known as *prototropic* tautomeric conversions.

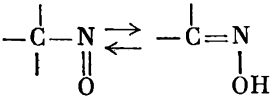
Besides the above-mentioned cases of keto-enol tautomerism and tricarbon tautomerism, proceeding as a termolecular process, prototropic tautomeric transformations include, for example*:



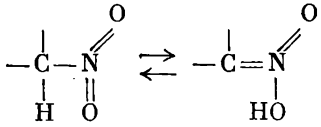
(Lactam-lactim tautomerism)



(Ketimide-enamine tautomerism)



(Nitroso-isonitroso tautomerism)

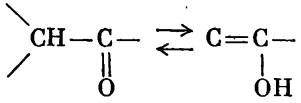


(Nitro-isonitro isomerism)

**Prototropy of Monocarbonyl Compounds.** In contrast to the cases of acetoacetic ester and diketones examined above, no tautomeric forms of monocarbonyl compounds have ever been isolated. A number of factors, however, suggest that prototropy may be possible in these compounds.

As halogenation reactions of monocarbonyl compounds have been studied very thoroughly, they will be used as models to prove the existence of prototropy in cases where tautomeric forms cannot be isolated.

The hypothesis of keto-enol tautomerism of monocarbonyl compounds

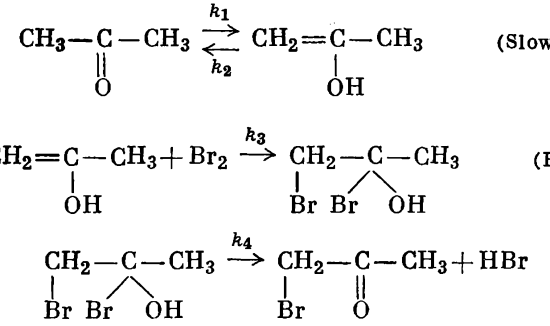


* The purpose of this chapter is to give a theoretical review of the problem of tautomerism as a whole, and not a description of individual tautomeric systems. The reader will find the latter in the book of I. Baker [12].

was put forward after it had been established that the rate of bromination of acetone in dilute aqueous solutions is proportional to the concentration of the ketone, but is independent of the concentration of the halogen [13]. It follows from this that the reaction proceeds in at least two steps, one of which (wherein the halogen participates) takes place so fast that its rate cannot be measured.

Then it was shown that the rate of bromination increases sharply if a mineral acid is added, which, therefore, accelerates the slow step of the reaction.

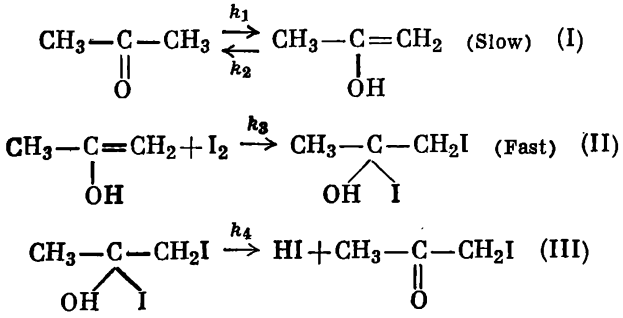
It follows from all these facts that the bromination of acetone is a two-step reaction: the slow step (catalyzed by acids) consists of the formation of the enol form of acetone, which then rapidly reacts with the bromine:



According to this supposition, the measured rate of bromination of acetone represents the rate of the prototropic tautomeric transformation. Thus the investigator acquires a convenient method of measuring the rates of prototropic tautomeric transformations, especially of those in which the second tautomer is unstable.

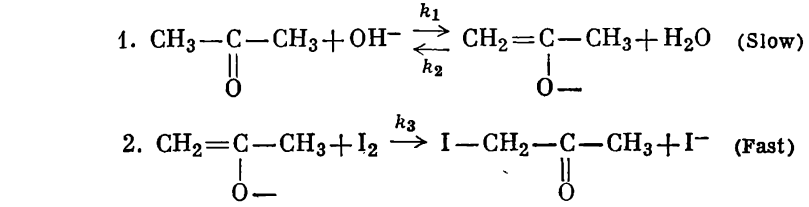
Investigations of the iodination of acetaldehyde and various ketones [14] confirmed that compounds of this type react with halogens in their enol forms.

The mechanism of acetone halogenation in an alkaline medium is different. The scheme



is not applicable in this case for the following reasons. Since the tautomeric constant of equilibrium (I) (page 658) is $2.5 \times 10^{-6}$, while the observed value of the acetone iodination rate constant under alkaline catalysis is of the order of $10^1$ $sec^{-1}$, it must be assumed that the rate constant of the second step (II) of the reaction ($k_3$) is about $10^6$-$10^7$ $sec^{-1}$ or more [15].

However, values of such a high order are not very probable for neutral organic molecules, and this indicates that the above scheme is incorrect. It is much more probable [16] that the halogenation of acetone in alkaline solution proceeds through an anion formed from the keto form rather than through the tautomeric enol form:

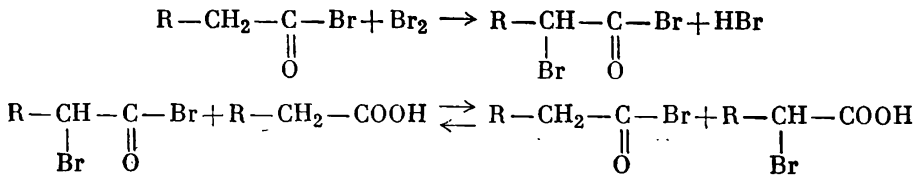


Here the second step of the reaction involves ions and not neutral molecules, therefore, it may be characterized by a rate constant of the order of $10^6$-$10^7$ or more.

The observed reaction constants of acetone halogenation in acid solution are of the order of $10^{-4}$ $sec^{-1}$ and $k_3$ is of the order of $10^1$ $sec^{-1}$. Rate constants of such an order are apparently possible for the molecular enol form. Therefore, the above mechanism of acetone bromination through the formation of the enol form of acetone is correct.

The mechanism of halogenation of acids is different. It was established [17] that in the bromination of acetic acid and its homologues the reaction rate depends on the concentration of the halogen [18], that the reaction is accelerated specifically by hydrogen halide acids, and not just by any acids at all, and that small amounts of the acid bromide increase the rate of bromination enormously, and this becomes proportional to the concentrations of both bromine and acyl bromide.

With these data taken into account, plus the well-known fact that acyl bromides are more readily halogenated than the corresponding acids (the Hell-Volhard-Zelinsky reaction is based on this), the following mechanism of bromination of acids suggests itself:



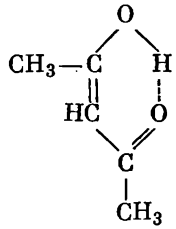
At first bromine reacts with the acid bromide to form an α-bromoacid bromide. The latter reacts with the initial acid yielding the acid bromide and the α-bromoacid. Chlorination proceeds by a similar mechanism [19].

Unlike monocarboxylic acids, malonic acid halogenates in the enol form; as in the case of acetone the rate of halogenation is independent of the halogen concentration. Moreover, the presence of enol in the malonic ester obtained by acidification of an alcoholic solution of sodiomalonic ester can be proved [20].

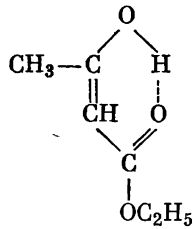
Bromination of succinic acid goes through the enol form [21]; the reaction is catalyzed by acids.

From the material presented in this section, as well as from previously presented material on keto-enol tautomerism, it is obvious that enol tautomers of different compounds may possess very different degrees of stability. The least stable are the enol forms of the simplest monocarbonyl compounds, such as acetone. The most stable are the enol forms of α- and β-diketones and of α- and β-ketocarboxylic acids in molecules possessing a system of conjugated double bonds.

An important factor determining the relative stability of the latter compounds is their ability to form intramolecular hydrogen bonds, e.g.:



Enol form of acetylacetone



Enol form of acetoacetic ester

### 10-1.4 Catalysis of Prototropic Transformations by Acids and Bases

The majority of prototropic transformations involving reactions of esterification and hydrolysis are catalyzed by both acids and bases.

On the basis that the catalytic activity of acids and bases is approximately proportional to their electrical conductance, Ostwald and Arrhenius put forward a hypothesis, according to which the catalytic action is due only to the hydrogen and hydroxyl ions. Confirmation of this hypothesis was given by the voluminous experimental material obtained by studying the hydrolysis rates of methyl and ethyl acetates under different conditions.

The Ostwald-Arrhenius hypothesis was not subjected to any serious criticism for 20 years (1887-1907) in spite of the fact that its experimental confirmation was but approximate and the catalytic effect of neutral salts could not be explained at all. However, from 1907 on a number of facts became known which could be understood only by assuming that prototropic transformations are catalyzed

not only by hydrogen and hydroxyl ions but by many other ions as well, and by undissociated molecules.

It was discovered that catalytic effect is produced by undissociated acids [22], anions of weak acids [23], a special case of which is hydroxyl ion, and also (in certain cases at least) by water molecules [24].

Thus, the rate of transformations taking place under the influence of acid-base catalysts in the aqueous phase is expressed by the following equation:

$$V = V_H + V_{OH} + V_M + V_A + V_{H_2O}$$

where $V_H$ = rate of catalysis by hydrogen ions;
$V_{OH}$ = rate of catalysis by hydroxyl ions;
$V_M$ = rate of catalysis by undissociated acid molecule;
$V_A$ = rate of catalysis by anions of weak acids;
$V_{H_2O}$ = rate of catalysis by water molecules.

All the catalysts mentioned above may be classified into two categories: those yielding protons ($H_3O^+$, undissociated acids) and those binding protons ($OH^-$, anions of weak acids, organic bases). Water combines both properties ($H_3O^+ \leftarrow H_2O \rightarrow OH^-$).

According to Brönsted [25] *acids* are proton donors, and *bases* are proton acceptors.

The relation between an acid and a base may be expressed as follows:

$$\text{Acid} \rightleftarrows \text{base} + H^+$$

(for example, $HCl \rightleftarrows Cl^- + H^+$ or $NH_4^+ \rightleftarrows NH_3 + H^+$)

An acid giving up a proton forms a *conjugate base* and, conversely, a base accepting a proton gives a *conjugate acid.**

Thus, at present the Ostwald-Arrhenius concepts of the catalysis of prototropic transformations by hydrogen and hydroxyl ions must be replaced by the concept of prototropic transformations by acids and bases in a general sense.

It is clear that if a reaction is catalyzed by acids and bases it must have a minimum value at a definite pH of the medium. Such a "minimum point" was actually discovered in the iodination of acetone, mutarotation of glucose and in the hydrolysis of esters.

The conditions existing at this "minimum point" may be calculated as follows [26].

Consider the acid-base catalyzed reaction taking place in aqueous solution in the presence of a constant concentration ($c$) of a weak acid HA (say, $CH_3COOH$) and a variable concentration of its salt.

While the salt concentration is very large, catalysis by the hydroxyl ion may be neglected as well as the minor catalytic effect of the water molecules.

* See Chapter 1 for details.

The rate equation may therefore be written as follows:

$$V=V_H+V_A+V_M=K_H[H^+]+K_A[A^-]+K_M[HA] \quad (1)$$

According to Ostwald's law of dilution

$$[H^+][A^-]=K(c-[H^+]),$$

hence,

$$V=K_H[H^+]+\frac{K_AK(c-[H^+])}{[H^+]}+K_M(c-[H^+])=$$

$$=(K_H-K_M)[H^+]+\frac{K_AK_c}{[H^+]}+(K_Mc-K_AK); \quad (2)$$

the last term may be neglected.

At the minimum point $dv/d[H^+]=0$, as a result of which the concentration of hydrogen ions at this point becomes equal to:

$$[H^+]_i=\sqrt{\frac{K_AK_c}{K_H-K_M}} \quad (3)$$

Substituting this expression into Equation (2), we obtain the rate at the minimum point:

$$V_i=2\sqrt{\{(K_H-K_M)K_AK_c\}}+K_Mc \quad (4)$$

From Equations (2) and (4) it follows that

$$(V_H)_i=(V_A)_i=\sqrt{\{(K_H-K_M)K_AK_c\}}$$

and the minimum point is thus characterized by equal effect of hydrogen ions and anions.

Let us consider now two equal rates on both sides of the minimum ("isocatalytic") point when the hydrogen ion concentrations are $[H^+]_1$ and $[H^+]_2$, respectively.

Equation (2) leads to the relation

$$(K_H-K_M)[H^+]_1+\frac{K_AK_c}{[H^+]_1}=(K_H-K_M)[H^+]_2+\frac{K_AK_c}{[H^+]_2}$$

Dividing both sides by $(K_H-K_M)$ and rearranging, we obtain:

$$[H^+]_1[H^+]_2=\frac{K_AK_c}{K_A-K_M}=[H^+]_i^2$$

$$(pH)_1+(pH)_2=2(pH)_i$$

The dependence of the rate on the pH should be represented by a symmetrical curve.

Remarkable agreement of calculations and experiment was obtained by Dawson and Dean [27] in a study of the iodination rate of acetone in the presence of acetic acid in different concentrations of sodium acetate. The results are shown in Fig. 10-1.

The general rate is represented by a solid curve, the broken lines representing the partial rates related to catalysis by hydrogen ions (curve $V_H$), by anions (curve $V_A$) and by undissociated molecules (curve $V_M$).

In studying the bromination of a number of halogenated acetones it was found that the position of the isocatalytic point depends

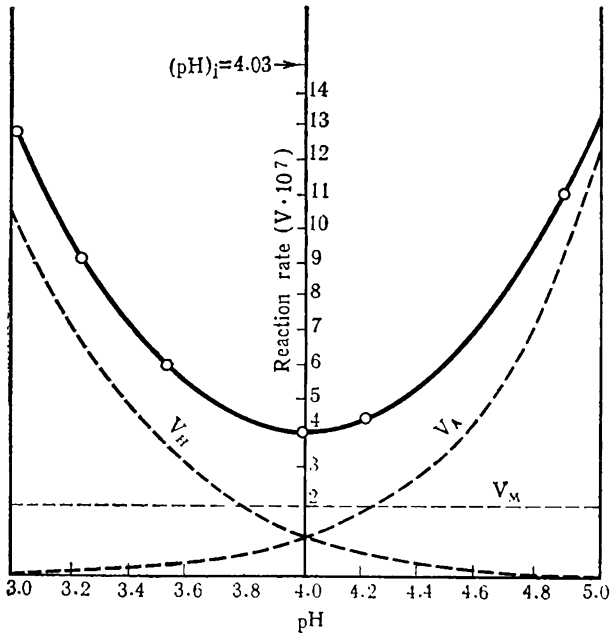
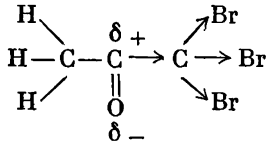



FIGURE 10-1 Rate of iodination of acetone in the presence of acetic acid and various concentrations of sodium acetate

on the number of halogen atoms in the acetone molecule. With increasing number of halogen atoms (for instance, in going from acetone to tetrabromoacetone) this point shifts continuously in the direction of higher acid concentration. In the case of the unsubstituted acetone the pH value is on the acid side of the isocatalytic point, and adding a mineral acid continuously increases the rate. In the case of monobromoacetone, unsymmetrical and symmetrical dibromoacetones, addition of a mineral acid at first lowers and then increases the rate. The minimum rate point in the three cases given above of bromosubstituted acetones is obtained by adding hydrochloric acid in concentrations of $0.002M$, $0.2M$ and $0.45M$, respectively. With $\alpha,\alpha,\alpha$-tribromoacetone the isocatalytic point is reached only when the concentration of hydrochloric acid is $2M$.

The shift of the isocatalytic point into the region of high acidity is due to the halogen atoms drawing electrons away from the carbonyl group, and thus making it more difficult for the proton catalyst to combine with the oxygen of the carbonyl group:



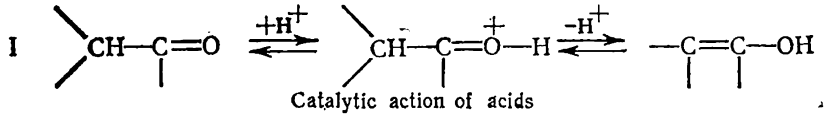
On the contrary, such compounds become much more amenable to attack by nucleophilic reagents, and therefore, prototropic transformations take place very readily under the action of basic catalysts.

### 10-1.5 Mechanism of Prototropic Transformations

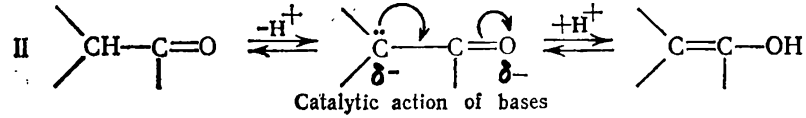
As early as 1890 a hypothesis was put forward, according to which tautomeric transformations take place through ionization of the mobile hydrogen atom [38]. This point of view is substantiated by the fact that strongly ionizing solvents facilitate the interconversion of tautomers [29].

Since prototropic transformations are catalyzed both by acids and alkalies, it is obvious that they may follow two different mechanisms.

As applied to prototropic transformations of carbonyl compounds he two mechanisms may be represented as follo ws [30]:



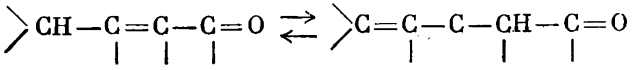
Catalytic action of acids



Catalytic action of bases

The initial step is the addition of proton to the oxygen of the carbonyl group (acid catalysis), or the loss of an α-hydrogen atom as a proton (basic catalysis).

An analogous mechanism has been suggested for keto-enol [31] and three-carbon [32] tautomerism. In the last case interconversion of isomers takes place only when the system is activated by the electronegative groups: carbonyl, carbethoxy, nitrile:



Basic catalysts are more effective in this case, but acid catalysts are also capable of causing the transformation.

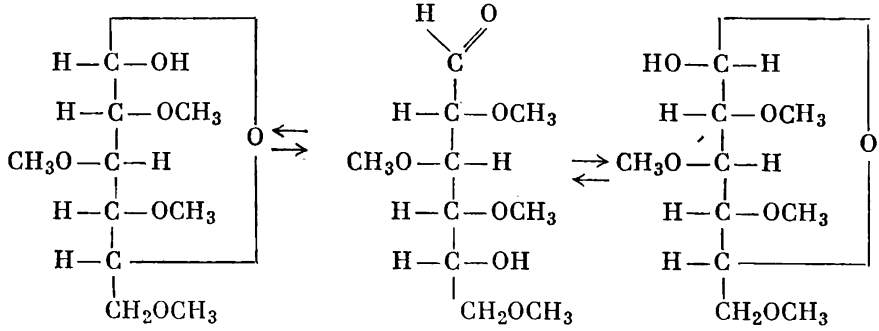
It is important to note that in accordance with the ionization theory [33] of prototropic transformations there is no fundamental difference between the acidic nature of a pseudo-acid (say, a ketone or a nitro compound) and of a true acid (such as an enol or an isonitro compound), because both groups are actual acids, though the former are much weaker than the latter.

When enols or ketones are ionized under the influence of basic catalysts the same enol anion $>C=\underset{|}{C}-O^-$ is formed with the negative charge concentrated mainly on the oxygen.

It should be pointed out that in such reactions as bromination of acetone it is unnecessary to postulate the intermediate formation of an enol. It is more probable (especially in basic catalysis) that an enol ion intermediate forms which reacts rapidly with the halogen (page 639), and the measured rate of the prototropic conversion which takes place under the action of alkalis is the rate of elimination of protons by the base [34].

As prototropic transformations provoked by bases proceed through the steps of proton addition and elimination, it may be expected that prototropic transformations take place only when there are a proton donor (acid) and a proton acceptor (base) present [35].

This assumption is confirmed by the results of a study of the mutarotation of tetramethyl glucose [36], which evidently consists of two prototropic transfomations:



In a chloroform solution tetramethyl glucose showed no change in the absence of a catalyst in ten days.

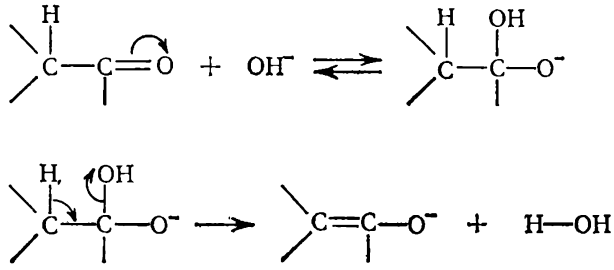
It was shown later that neither pyridine (an acceptor of protons), nor cresol (a donor of protons) catalyze mutarotation separately, but their simultaneous presence has a strong catalytic effect [37].

In the absence of impurities there is a long induction period in the bromination of acetone and keto acids in non-aqueous solvents

(from 10 minutes to several hours). The reaction probably begins only when impurities able to catalyze the transformations get into the reaction mixture.

The above concepts of the mechanism of prototropic transformations agree well with experimental data and are generally accepted at present.

For base-catalyzed prototropic transformations another equally probable mechanism has been suggested [38]:



According to this mechanism the rate of prototropic transformation depends on two factors, specifically, on the rate of reaction of the ketone with the catalysts and on the stability of the product of addition of the catalyst to the ketone.

### 10-1.6 Mechanism of Anionotropic Transformations

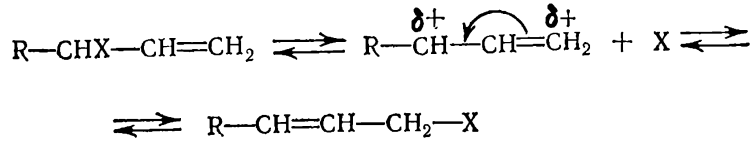
Anionotropic transformations have been studied less than prototropic ones.

On the basis of a study of the interconversion of α-phenylallyl alcohol $C_6H_5-CHOH-CH=CH_2$ and cinnamyl alcohol $C_6H_5-CH=CH-CH_2OH$, Barton and Ingold [39] formulated a series of general propositions concerning the mechanism of anionotropic transformations.

It was discovered that if refluxed in acetic anhydride α-phenylallyl *p*-nitrobenzoate changes smoothly into cinnamyl *p*-nitrobenzoate:

$$C_6H_5-CHX-CH=CH_2 \rightarrow C_6H_5-CH=CH-CH_2X$$
$$(X = p\text{-}O_2NC_6H_4COO)$$

Since a mixture of cinnamyl-*p*-nitrobenzoate and cinnamyl acetate forms in the presence of tetramethylammonium acetate, it is evident that in the course of the conversion complete elimination of $X^-$ occurs with the formation of a kinetically independent cation. Anionotropic conversion, therefore, may be represented as follows:



Anionotropic conversion is favoured by three factors:

1. The ability of X to form a stable anion. Thus, alcohols (X = = OH) do not interconvert, but acetate esters (X = $OCOCH_3$), and the more so bromides (X = Br) display a tendency for anionotropy.

2. An increase in the ionizing strength of the medium facilitates anionotropic transformations.

3. Anionotropy is favoured by an increase in the electron-donor properties of the R group:

$$H < CH_3 < C_6H_5 < n\text{-}CH_3C_6H_4$$

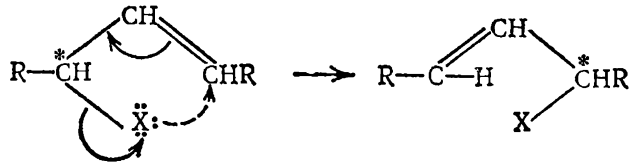
This is due to the increasing stability of the cation

$$[R \longrightarrow CH \cdots\cdots CH \cdots\cdots CH_2]^+$$

because the positive charge becomes still less localized (partial positive charges are acquired by the corresponding atoms of the group R).

The mechanism of the anionotropic transformations which take place in ionizing solvents is similar to the mechanism of monomolecular nucleophilic substitution at a saturated carbon atom ($S_N1$).

Anionotropic transformations taking place in nonpolar solvents or without a solvent, apparently follow a different mechanism, analogous to $S_N2$:



If the initial compounds in such anionotropic transformations are optically active, their optical activity is retained.

In general, anionotropic transformations may follow both mechanisms simultaneously (similarly to $S_N1$ and $S_N2$).

For example in the reaction:

$$C_6H_5-\overset{*}{C}HX-CH=CH-CH_3 \longrightarrow C_6H_5-CH=CH-\overset{*}{C}HX-CH_3$$
$$(X = OH,\ o\text{-}HOOCC_6H_4COO-)$$

70% of the optical activity is retained. It is probable that the reaction follows an ionic mechanism with racemization to an extent of 30%.

When a group X in the anionotropic system is replaced by a group 1Y, the entering group may join the carbon atom with which the eaving group X was bound, or with another carbon atom[1].

[1] Involving a transfer of the reaction centre (page 60).

Substitution may be either single-step (mechanism II), or two-step (mechanism I), when Y adds to the cation after the departure of X:

$$R-CHX-CH=CH_2 \longrightarrow X^- + [R-CH \cdots CH \cdots CH_2]^+$$

$$Y^- + [R-CH \cdots CH \cdots CH_2]^+ \begin{cases} \longrightarrow R-CHY-CH=CH_2 \\ \longrightarrow R-CH=CH-CH_2Y \end{cases} \quad (I)$$

$$Y^- + R-CHX-CH=CH_2 \begin{cases} \longrightarrow X^- + R-CHY-CH=CH_2 \\ \longrightarrow X^- + R-CH=CH-CH_2Y \end{cases} \quad (II)$$

If the substitution follows mechanism I, then under identical conditions the isomeric initial compounds R — CHX — CH = $CH_2$ and R — CH = CH — $CH_2X$ should give the same mixtures of isomeric end products in the reaction with Y*. In the reaction proceeding according to mechanism II the same mixture of end products should not form.

This made it possible to confirm experimentally the existence of two different substitution mechanisms in anionotropic systems.

## 10-2 DUAL REACTIVITY AND TAUTOMERISM

### 10-2.1 Reasons for Dual Reactivity

As was shown above, a large number of allelotropic mixtures have been successfully separated by isolating individual tautomers ("desmotropic" forms). In the case of many keto-enols, though separation of desmotropic forms in the pure state has not been accomplished, their existence in solutions or melts has been proved by means of physico-chemical methods. All these materials possess dual reactivity.

It is not surprising that the seemingly reasonable assumption was put forward later, that the cause of dual reactivity of any substance whatever is due to the existence of two (or more) desmotropic forms, each of which yields its own series of derivatives.

Thus, dual reactivity became accepted as a necessary and sufficient indication of tautomerism.

Kurt Meyer [40] defines tautomerism as follows: "Substances are tautomeric if they form two series of derivatives from the two isomeric formulas; these formulas differ from each other in the position of a hydrogen atom and of one or more double linkages."

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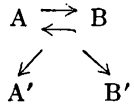
* Cf. page 592.

Schlenk and Bergman define tautomerism as dynamic isomerism of two desmotropic forms, and then add [41]:

"Besides, we may speak of tautomerism when a compound gives two series of derivatives, corresponding to the above-mentioned forms, though the compound itself may be known in one form only."

Shorygin wrote on this question [42]: "The current definition of tautomerism is: a phenomenon wherein an organic compound yields two series of derivatives, corresponding to two initial structural formulas, which differ from each other mainly in the position of one or several hydrogen atoms in the presence or absence of one or several double bonds, the compound in its free state not being separable into its isomeric forms, and the existence of the two forms being suggested only by its reactions."

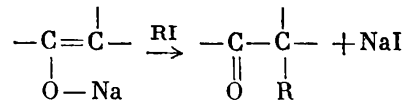
Tautomerism became completely identified with dual reactivity when it was admitted a priori that whenever two series of derivatives are formed, all the derivatives possessing the structure of one of the possible tautomeric forms are produced specifically from it, and all the derivatives, having the structure of the second tautomeric form are produced from the second form. This hypothesis may be illustrated schematically:



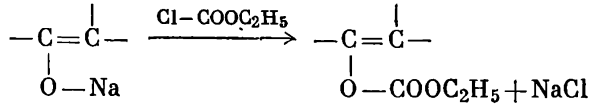
In recent years Nesmeyanov *et al.* have shown [43, 44], that the phenomenon of dual reactivity is broader than tautomerism and is stipulated in general by the specific features of molecules with conjugated bonds.

This question was investigated the most thoroughly with respect to metallic derivatives of keto-enol systems.

It is known that alkali salts of keto-enols exist as salts of the enol forms. No case of structural isomerism of the salts of keto-enols, derived from a difference in the position of the metal, is known. Neither is any sodium or potassium derivative of the keto form of the keto-enols known. At the same time, all reactions of alkylation of alkali (or other) salts of keto-enols result in C-derivatives, i.e., derivatives of the keto form of the substance:

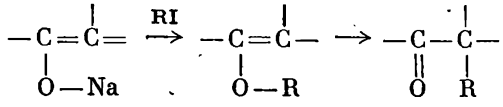


Only a few reactions of acylation (e.g., with a chlorocarbonate ester) result in O-substitution:



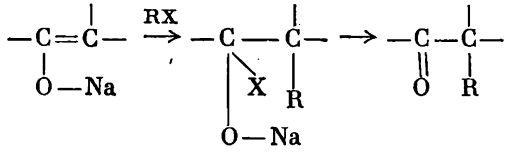
Therefore, this case involves dual reactivity, which is difficult to account for if we consider ketonic derivatives to be formed from keto forms, and enolic derivatives from enol forms.

To preserve this hypothesis various arbitrary assumptions were made at different times. Claisen assumed [45] initial O-substitution followed by a rearrangement:



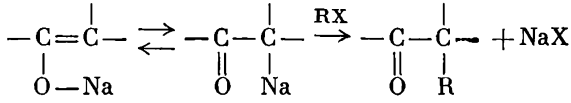
However, this hypothesis was contradicted by the inability of simple enolic ethers to undergo such a rearrangement [46].

Michael's hypothesis [47] consisted in assuming that initially alkyl halide adds to the double bond of the enolate with subsequent elimination of NaX:



However, this hypothesis was disproved because of the inability of alkyl halides to add to double bonds under the conditions of alkylation of the keto-enols (ethereal or alcoholic medium, presence of alcoholate, etc.) [48].

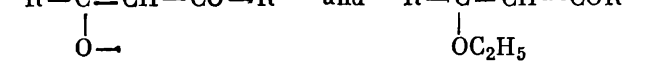
Hückel assumed pseudomerism of alkali enolates:



However, this hypothesis is not valid either: it involves admission of the existence of organometallic derivatives of the keto forms, the sole evidence of which is the phenomenon of C-alkylation, which it is required to explain. We have here, therefore, a vicious circle.

Finally Arndt and Eistert [49] have developed the concept of ionic reactions of salts of tautomeric substances. According to this concept, it is not the undissociated keto-enolic salt that takes part in the reaction of alkylation or acylation, but its anion, the charge of which is divided among the oxygen and carbon atoms ("mesomeric" ion). Accordingly, electrophilic reagents may attack not only the oxygen atom, but the carbon atom as well, and depending on the nature of the reagent and the conditions of reaction may form C- or O-derivatives.

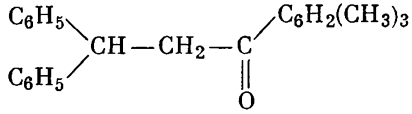
It should be noted first of all that the anions of β-dicarbonyl compounds, are evidently not "mesomeric", but enolatic in structure (perhaps with a slightly greater electronic density on the carbon atom). Their spectral properties greatly resemble those of the corresponding O-alkyl derivatives of enols:



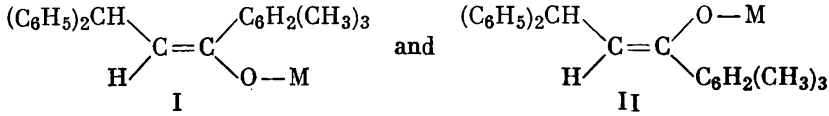
Consequently, both O- and C-derivatives must form from the anion of enolate structure. Finally, it must be taken into consideration that metallic derivatives of keto-enol systems, as will be shown below, are capable of exhibiting dual reactivity under conditions obviating anion formation.

Thus, within the framework of the proposition that each tautomeric form yields derivatives corresponding to its structure, and, consequently, of the more general hypothesis that dual reactivity and tautomerism are fully coinciding phenomena, it is impossible to find a contradiction-free explanation of the numerous facts of dual reactivity of the metallic derivatives of keto-enols.

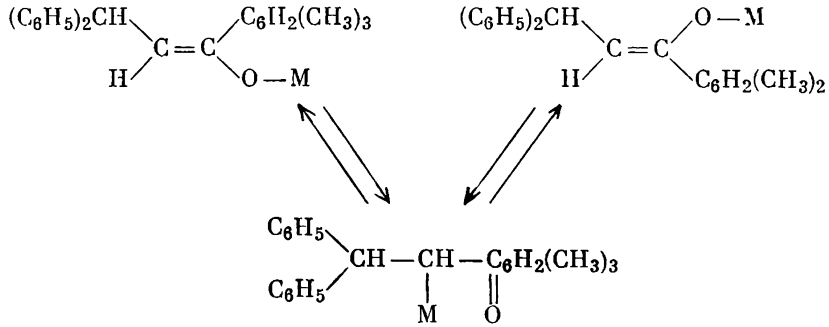
Nesmeyanov, Sazonova *et al.* [50] investigated the dual reactivity of metallic (lithium, magnesium and sodium) derivatives of diphenylpropiomesitylene:



They proved convincingly that the metallic derivatives of diphenylpropiomesitylene have an enolic structure, because they exist in two stereoisomeric I and II (*cis-* and *trans-*) forms:



It was shown further, that under definite investigated conditions these stereoisomers are incapable of interconversion, and, therefore, there is no keto-enol tautomerism involved. If keto-enol tautomerism existed in metallic derivatives of diphenylpropiomesitylene (as was postulated by Hückel for sodium acetoacetate) both stereoisomeric enolates could interconvert through the keto form:

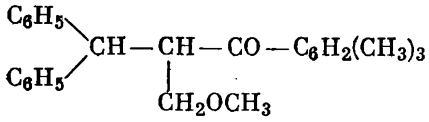


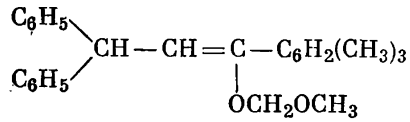
Finally, it was shown that in enolates the bond between oxygen and the metal is not ionic $= \overset{|}{C} - O^{-}Me^{+}$, but covalent $= \overset{|}{C} - O -$ — Me. Whenever this bond becomes ionic, *cis-trans*-isomerism disappears.

For instance, if Li, Na or Mg are replaced by $(CH_3)_4N^{+}$, the bond of the latter with oxygen will naturally be ionic $= \overset{|}{C} - O^{-}\overset{+}{N}(CH_3)_3$; after this it is no longer possible to isolate *cis-trans*-isomers.

Thus, the reasons for the dual reactivity of metallic derivatives of keto-enols should not be sought in the properties of the "mesomeric" anion as was postulated by Arndt and Eistert, but in the properties of covalently bound enolates.*

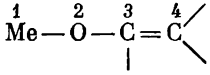
Dual reactivity is characteristic of the stereoisomeric enolates of diphenylpropiomesitylene: they are capable, under corresponding conditions, of forming C- and O-derivatives on alkylation and on acylation, e.g.:



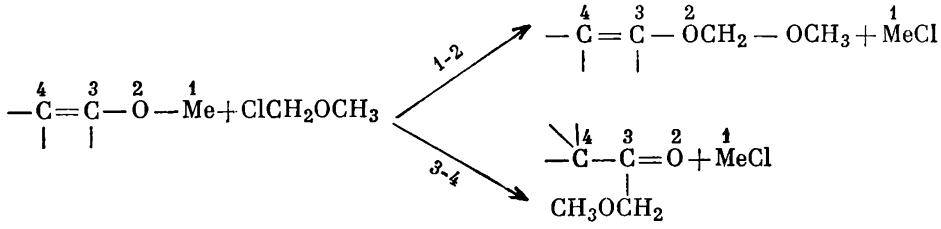


The O-derivatives form as two stereoisomers, corresponding in steric configuration to the original enolates. Thus, benzoylation of sodium enolate I results in one benzoyl derivative, and benzoylation of sodium enolate II — in another stereoisomeric benzoyl derivative. Each stereoisomer is obtained free from any admixture of the other. On saponification both benzoyl derivatives form the original diphenylpropiomesitylene. Ketonic derivatives always give one form, independent of which enolate stereoisomer was used in the reaction.

These investigations of Nesmeyanov *et al.* show that equilibrium isomerism is not a prerequisite of dual reactivity (ability of the anolates mentioned to form C- and O-derivatives). Dual reactivity in these and in many other cases has a different reason. According to the views of Nesmeyanov it takes place because of the presence in the molecules of a conjugated system of single and double bonds. In the case at hand:



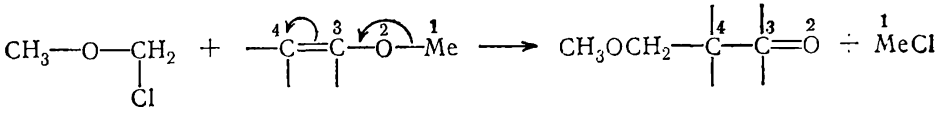
the existence of bond conjugation determines the capacity for dual reaction on bonds 1-2 or 3-4:



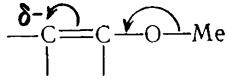
In the first case the substitution reaction occurs at the atom of the molecule, from which the substituent (metal atom) leaves.

* See, however, the footnote on page 64.

In the second case a new substituent joins the carbon atom which is at the other end of the conjugated system. Nesmeyanov calls reactions of the latter type reactions involving *transfer of the reaction centre.*



The acyl or alkyl cation (the new substituent) attacks the carbon atom to which the electronic pair released upon rupture of the oxygen-metal bond and necessary for the new bond is transferred at the moment of reaction. The action of the conjugated systems thus consists in an easily caused displacement of the electron pairs 1-2 and 3-4. Even if some partial negative charge is assumed to be present on the fourth carbon atom of the non-reacting system (this charge cannot but be insignificant)

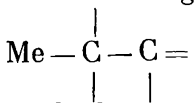


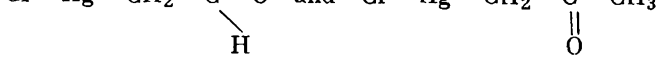
even then additional displacement of electrons will necessarily take place at the moment of reaction.

Thus, the case of metallic derivatives of diphenylpropiomesitylene yielded experimental proof of the possibility of formation of two series of derivatives *without dynamic isomerism.*

It follows from the same experimental data that the rule, according to which ketonic derivatives are obtained from the keto form and enolic from the enol form, is not always true. Both ketonic and enolic derivatives of diphenylpropiomesitylene have been obtained from enol forms.

It is quite possible that analogous relations exist in the case of metallic derivatives of other tautomeric forms, for example, lactim-lactam. Their metallic derivatives are apparently in the lactim form, but are capable of forming either lactim or lactam derivatives in different reactions.

Dual reactivity of metallic derivatives having, to a certain degree, the reverse system of atoms  was studied by Nesmeyanov, Lutsenko and Perevalova [51] using organomercury compounds of aldehydes and ketones. α-Mercuriated hydroxy compounds, e.g., chloromercuryacetaldehyde and chloromercuryacetone



are doubtlessly true organomercury compounds. This is borne out, for instance, by the fact that when treated with alkali they do not release mercury oxide, and when reduced they give the corresponding mercuriated alcohols, for example:

$$\mathrm{ClHg{-}CH_2{-}\underset{\underset{H}{|}}{C}{=}O} \longrightarrow \mathrm{ClHg{-}CH_2{-}CH_2{-}OH}$$

Tautomerism of these compounds

$$\mathrm{ClHg{-}CH_2{-}\underset{\underset{O}{\|}}{C}{-}CH_3} \rightleftarrows \mathrm{CH_2{=}\underset{\underset{OHgCl}{|}}{C}{-}CH_3}$$

does not occur, which is confirmed by the stability of α-mercuriated ketones to cold permanganate solution. It is clear that these compounds are not in equilibrium with the isomeric mercury enolates, because the latter would certainly have been oxidized.

Having a ketonic structure, α-mercuriated keto compounds possess the specific dual reactivity of keto-enols. While in the reaction with bromine the mercury atom is replaced by bromine to form a C-derivative

$$\mathrm{ClHg{-}CH_2{-}CHO + Br_2} \longrightarrow \mathrm{Br{-}CH_2{-}CHO + HgClBr},$$

with many acyl halides these compounds form oxygen derivatives (vinyl esters)

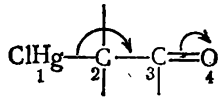
$$\mathrm{ClHg{-}CH_2{-}C\begin{smallmatrix}\nearrow O\\ \searrow H\end{smallmatrix}} + \mathrm{Cl{-}\underset{\underset{O}{\|}}{C}{-}R} \longrightarrow \mathrm{CH_2{=}CH{-}O{-}\underset{\underset{O}{\|}}{C}{-}R + HgCl_2}$$

Of interest is their relation to triphenylmethylchlorides, the reaction with which may result in C- or O-derivatives, depending on the nature of the halogen compound:

$$\mathrm{ClHg{-}CH_2{-}CHO} \begin{cases} \xrightarrow{(C_6H_5)_3CCl} (C_6H_5)_3C{-}CH_2{-}CHO + HgCl_2 \\ \xrightarrow{(NO_2C_6H_4)_3CBr} CH_2{=}CH{-}O{-}C(C_6H_4NO_2)_3 + HgClBr \end{cases}$$

Since the mercury atom is bound with carbon in these cases, it is obvious that in the formation of O-derivatives the reaction takes place, in the examples given, with transfer of the reaction centre and the reason for the dual reaction is not tautomeric equilibrium but

the presence of σ-, π-conjugation of the 1-2 and 3-4 bonds:



The difference from the metallic derivatives of diphenylpropiomesitylene is that here both ketonic and enolic derivatives originate from keto forms.

An extensively studied class of substances, exhibiting dual reactivity in the absence of tautomerism are compounds of heavy metal salts with unsaturated compounds (acetylenes, olefins, carbon monoxide).

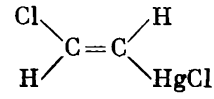
β-Chlorovinylmercury chloride (I), obtained by the addition of mercuric chloride to acetylene [52], and di-β-chlorovinylmercury (II), formed by the action of ammonia on β-chlorovinylmercury chloride [53]:

$$\underset{\text{(I)}}{ClCH=CH-HgCl} \qquad \underset{\text{(II)}}{(ClCH=CH)_2Hg}$$

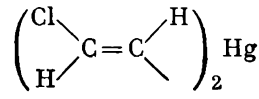
are doubtlessly true β-chlorovinyl organometallic derivatives, because in many exchange reactions the HgCl group is replaced:

$$ClCH=CH-HgCl+I_2 \longrightarrow ClCH=CHI+HgCII$$
$$ClCH=CH-HgCl+Cl_2 \longrightarrow ClCH=CHCl+HgCl_2$$
$$ClCH=CH-HgCl+HBr \longrightarrow ClCH=CH_2+HgClBr$$
$$(ClCH=CH)_2Hg+ICl_3 \longrightarrow ClCH=CHICl_2+ClCH=CH-HgCl$$

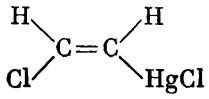
Stable *cis-trans*-isomers have been obtained for both chlorovinylmercury chloride and dichlorovinylmercury:



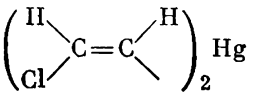
*trans*



*trans*



*cis*



*cis*

Meanwhile, in a number of reactions, all these compounds readily eliminate acetylene by splitting off the elements of mercuric chloride. This occurs, for example, if the substances are heated above their melting points.

$$(ClCH=CH)_2Hg \longrightarrow ClCH=CH-HgCl+H-C\equiv C-H$$
$$ClCH=CH-HgCl \longrightarrow HgCl_2+H-C\equiv C-H$$

Acetylene can be eliminated still easier, even at room temperature, by treating all four compounds with many reagents capable of binding mercuric chloride in one way or another (potassium iodide, potassium cyanide and others).

Reactions resulting in the elimination of acetylene resemble those of organomagnesium and organotin compounds with diazomethane:

$$C_2H_2HgCl_2 + C_6H_5MgBr \longrightarrow C_2H_2 + C_6H_5HgCl + MgClBr$$

$$C_2H_2HgCl_2 + 2C_6H_5SnCl_3 \xrightarrow{NaOH} C_2H_2 + (C_6H_5)_2Hg + Na_2SnO_3$$

$$C_2H_2HgCl_2 + CH_2N_2 \longrightarrow C_2H_2 + ClCH_2HgCl + N_2$$

In these cases chlorovinylmercury chloride and dichlorovinylmercury behave like mercuric chloride, bound complexly with acetylene.

Thus, chlorovinyl organomercury compounds exhibit dual reactivity. Depending on the nature of the reagent and the conditions of the reaction they behave like true organometallic compounds or like complex compounds.

Similar dual reactivity is observed in chlorovinyl derivatives of antimony [54], tin [55], lead [56], thallium [57] as well as in the addition products of mercury to olefins [58] and carbon monoxide [59].

The reactivity of many products of addition of metal salts to acetylene and to olefins (named "quasicomplex compounds" by Nesmeyanov) is so much alike that the reasons for their specific properties determining their resemblance to complex compounds must be general.

It is clear that these reasons cannot lie in a new type of tautomerism—reversible isomerism of a true chlorovinyl organometallic compound into a true complex, e.g.,

$$ClCH{=}CH{-}HgCl \rightleftarrows C_2H_2 \cdot HgCl_2$$

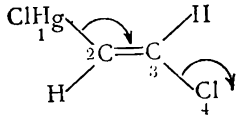
because if this were so the existence of stable *cis-trans*-isomers of chlorovinyl organometallic compounds would be impossible. For the same reason it is impossible to assume the existence of a mobile equilibrium of adducts with the products of their dissociation, e.g.:

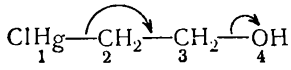
$$ClCH{=}CH{-}HgCl \rightleftarrows H{-}C{\equiv}C{-}H + HgCl_2$$

Consequently, in the case of quasicomplex compounds we come again upon dual reactivity due to causes other than by tautomerism.

These causes are the ability of the 1-2 and 3-4 bonds to polarize readily under the influence of the attacking reagent. The electronic

shifts in these cases occur in the directions shown by the bent arrows.





Reactions involving elimination of a hydrocarbon (acetylene, ethylene) which are unusual for organometallic compounds are caused precisely by this kind of ready polarizability[1] of the conjugated 1-2 and 3-4 bonds.

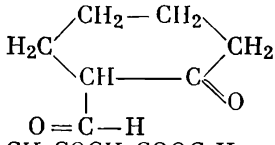
It follows therefore that dual reactivity is not always a result of tautomerism. The phenomenon of dual reactivity is broader and more prevalent than the phenomenon of tautomerism. Therefore, it is more correct to regard as tautomerism only the sphere of phenomena foreseen by Butlerov—the sphere of reversible isomerization equilibria.

## 10-2.2 Tautomeric Equilibrium

Tautomeric equilibrium is characterized by its position and the rate at which it is established in different media. Both the positions and the rates of establishment of tautomeric equilibria differ widely for different substances as is shown in Tables 10-1 and 10-2:

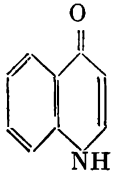
TABLE 10-1

**Constants of Tautomeric Equilibrium**

| Substance | Constant of tautomeric equilibrium in aqueous solution* $K_{T,\,H_2O} = \frac{C_e}{C_k}$ |
|---|---|
|  | 0.94 |
| $CH_3COCH_2COOC_2H_5$ | $4 \times 10^{-3}$ |

[1] This effect is apparently almost exclusively dynamic and develops at the moment of reaction; a study of Raman spectra shows that molecules of β-chlorovinyl organometallic compounds have a double bond without a trace of triple linkage [60].

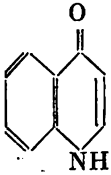
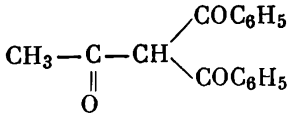
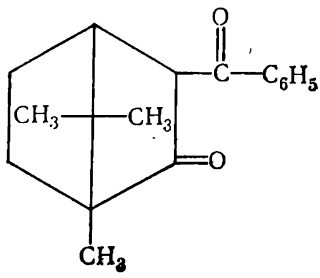
*(Continued)*

| Substance | Constant of tautomeric equilibrium in aqueous solution $K_{T,H_2O}=\frac{C_e}{C_k}$ |
|---|---|
| $CH_3COCH(CH_3)COOC_2H_5$ | $9\times10^{-4}$ |
|  | $7.8\times10^{-5}$ |
| $CH_3COCH_3$ | $2.5\times10^{-6}$ |
| $CH_3NO_2$ | $4\times10^{-8}$ |

*$C_e$ and $C_k$ are the concentrations of the enol and keto forms, respectively.

TABLE 10-2

**Ease of Interconvertibility of Isomeric Forms**

| Substance | Ease of interconvertibility of isomeric forms |
|---|---|
|  $CH_3COCH_2COCH_3$ | Equilibrium established practically instantaneously. Isomers cannot be isolated under any conditions |
|  | Equilibrium attained in 20-30 min at room temperature. Isomers can be isolated at −70° |
|  | Equilibrium attained in the course of several weeks. Isomers stable under ordinary conditions |

The rate of establishment of tautomeric equilibrium depends on the nature of the solvent (see, for example, Table 10-3) and is affected by catalysts.

TABLE 10-3

**Percentages of Enol Form in Solutions of Acetoacetic Ester in Different Solvents at 18°**

| Solvent | Per cent of enol | Solvent | Per cent of enol |
|---|---|---|---|
| Water . . . . . | 0.40 | Acetone . . . . . | 7.3 |
| Methanol (25%) . . . | 0.83 | Chloroform . . . . . | 8.2 |
| Methanol (50%) . . . | 1.52 | Nitrobenzene . . . . | 10.1 |
| Ethanol (50%) . . . | 2.18 | Ethyl acetate . . . . | 12.9 |
| Methanol . . . . . | 6.87 | Benzene . . . . . | 16.2 |
| Ethanol . . . . . | 10.52 | Ethyl ether . . . . . | 27.1 |
| Propanol . . . . . | 12.45 | Carbon disulphide . . | 32.4 |
| Amyl alcohol . . . . | 15.33 | Hexane . . . . . | 46.4 |

The laws of tautomeric equilibrium in dilute solutions have been found experimentally. On the basis of a large amount of experimental material, Kurt Meyer [61] established that the tautomeric equilibrium constant is proportional to the constant of enolization of the substance in question and to a constant characterizing the enolizing power of the solvent used.

$$K_T = EL \text{ (K. Meyer's formula)}$$

where $K_T$ = tautomeric equilibrium constant;
$E$ = "enolization constant", characteristic of each tautomeric substance;
$L$ = constant characterizing the "enolizing power" of the solvent.

Acetoacetic ester was adopted by Meyer as the reference standard in all solvents; therefore, its $E = 1$.

The values of $E$ for different tautomeric substances are listed in Table 10-4*.

The second important relationship characterizing tautomeric equilibrium in dilute solutions was discovered by Dimroth [63]. Dimroth's formula relates the position of equilibrium to the solubility of the isomeric forms:

$$K_T = G \frac{L_e}{L_k}$$

* The numerical data of Tables 10-1, 10-2 and 10-4 were taken from the work of Kabachnik [62].

TABLE 10-4

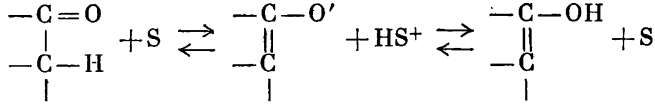
**Enolization Constants of Different Compounds**

| Substance | *E* | Substance | *E* |
|---|---|---|---|
| Methyldibenzoylmethane | 0.02 | Acetylcamphore | 7.0 |
| Ethylacetoacetic ester | 0.23 | Tribenzoylmethane | 10 |
| Methylbenzoylacetone | 0.6 | Benzoylcamphore | 12 |
| Acetoacetic ester | 1.00 | 3-Bromacetylacetone | 22.5 |
| Benzoylacetic ester | 2.3 | Acetylacetone | 33 |
| 2-Methylindanedione | 2.75 | Benzoylacetone | 120 |
| Indanedione-1,3 | 3.75 | Dibenzoylmethane | 350 |
| | | Dimedone | 5,075 |

where $K_T$ = tautomeric equilibrium constant;
$L_k$ and $L_e$ = solubilities of keto and enol forms in a given solvent;
$G$ = constant, characteristic of the solvent.

Dimroth's formula is applicable not only to tautomeric but to any chemical equilibrium [64].

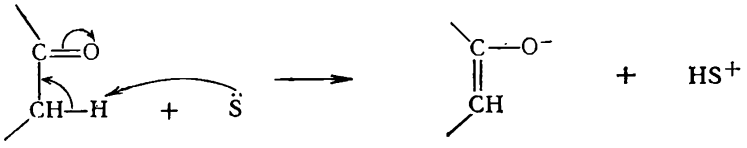
Numerous investigations of tautomeric keto-enol equilibria in solutions indicate that they are acid-base equilibria of two acids—a ketone and an enol—which ionize into the same anions of enolate structure [65, 66]. The proton is transferred from the ketone to the enol and back through the agency of a third kind of molecules—proton-transfer agents S—capable of reversible addition of proton.



The proton-transfer agents (S) may be any particles possessing proton affinity. They may be solvent molecules, if the latter possess basic properties (water, alcohols, ethers), anions of solvents (hydroxide anions in water, acetate anions in acetic acid which, as is well known, possess strongly basic properties); they may be molecules of any base present in solution (pyridine, amines, etc.). Finally in aprotic solvents, such as benzene, carbon disulphide, hydrocarbons, the proton-transfer agents S may be the molecules of keto-enol due to their ability to add protons. In all cases the role of the particles S is the same and consists in removal of a proton from one of the atoms of the organic molecule (e.g., from the methylene group of the ketone) followed by addition of the proton to another

atom of the anion formed (e.g., to the oxygen of the enolate anion), and vice versa.

At one of the stages of tautomeric transformation the process involves transfer of the reaction centre. Namely, when proton is removed from the keto form, the negative charge does not develop on the carbon atom, from which the proton was eliminated, but on the oxygen atom located at the other end of the conjugated system H — C — C = O:



On recombination of the ions to assume the keto form

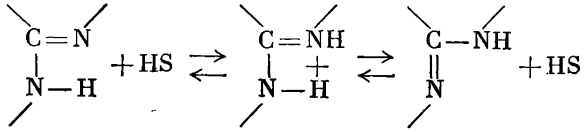
the proton, likewise, does not add to the oxygen atoms on which the negative charge is concentrated (or nearly concentrated), but to the carbon atom located at the other end of the conjugated system O — C = C.

Ionization of the enol form and reverse recombination of the ions to assume the enol form does not involve transfer of the reaction centre: the ionic charge arises and then is neutralized on the same atom of the molecule from which the proton was eliminated and to which it was later added. Proton removal from the enol form is rapid; from the keto form it is slow (pseudo-acid).

Physico-chemically, tautomeric keto-enol equilibrium is a complex case of acid-base protolytic equilibrium in solution; it differs from ordinary acid-base equilibria, first, in that two acids, instead of one as usual, give rise to the same type of anion, so that the anion possesses two different basicity constants (for addition of the proton to two different atoms of the anion), and second, in that one of the acids participating in the equilibrium (namely, the keto form), is a pseudo-acid, the ionization of which is slow. In other respects, keto-enol equilibrium is subject to the same laws as the ionization equilibrium of ordinary weak acids.

The above concept of tautomeric keto-enol equilibrium is doubtlessly applicable also to other types of prototropic equilibrium of acidic substances. It should be pointed out that pseudo-acidity is not necessarily a characteristic feature of tautomeric equilibrium

of acids: in lactim-lactam tautomerism, for instance, both forms are true acids. It should also be noted that concepts of this kind must also be applicable to prototropic tautomerism of basic substances. Here proton transfer is not accompanied by the formation of a common anion, but of a common cation, evolved by both tautomeric forms as a result of proton addition to each of them at the different ends of the conjugated system of atoms. This is the case, for example, in amidine tautomerism:



It is possible that tautomeric keto-enol transformation in acid solution (e.g., in sulphuric acid [67] or in general on acid catalysis of keto-enol transformation) also follows such a mechanism.

The mechanism of establishment of keto-enol equilibrium may be expressed by the following scheme:

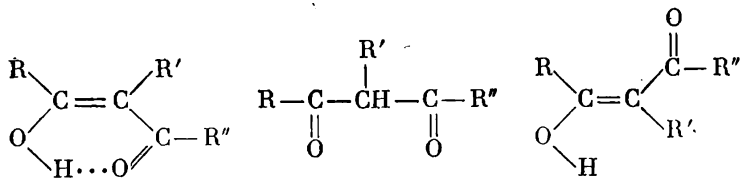
$$KH + S \rightleftarrows A^- + HS^+ \rightleftarrows EH + S$$

where KH = ketone;
EH = enol;
$A^-$ = anion common to ketone and enol;
S = a base.

Kabachnik [68, 69] applied the theory of acid-base equilibrium developed by Brönsted [70] and recently by Izmailov [71] to the calculation of tautomeric equilibria. He confirmed the above mechanism of establishment of tautomeric equilibrium and derived several basic quantitative relationships, characterizing tautomeric equilibrium (and, in particular, Meyer's formula).

It was thus shown that certain laws of acid-base equilibrium derived for ordinary acids and bases are fully applicable to ketones, enols and acids. Equations derived in this manner are of great importance because they enable quantitative study of tautomeric keto-enol transformations.

It should be noted, finally, that in the general case of open chain β-dicarbonyl compounds in solutions there are at least three forms in equilibrium: ketonic, *cis*-enolic and *trans*-enolic [72].



*cis*-Enol form Keto form *trans*-Enol form

The equilibrium of these three forms depends on the ratios of their ionization constants in any given solvent, which in their turn depend on the "acidities of the forms proper" and their solvation [66, 73, 74].

### 10-2.3 Dual Reactivity of Tautomeric Substances with Strongly Displaced Equilibrium

As was shown for the metallic derivatives of keto-enols, dual reactivity is not dependent on the existence of tautomerism. A metallic derivative has a definite structure (e.g., enolate in the case of diphenylpropiomesitylene), but reacts dually (with and without transfer of the reaction centre), forming derivatives of enolic, as well as ketonic structure.

If a substance is tautomeric, the simplest supposition is that the keto form should give ketonic derivatives and the enol form, enolic derivatives (see page 633).

The actual relationships were shown by Kabachnik [62] to be much more complex.

First let us consider the cases of strongly displaced tautomeric equilibria. To explain dual reactivity in substances for which it was not found possible by any means to establish tautomeric equilibrium, the concept of pseudomerism was put forward.

According to Knorr [81] pseudomerism implies a maximally displaced tautomeric equilibrium where the concentration of one of the forms is "vanishingly" small, but the molecules of this form are very reactive. In such a case, rapidly established equilibrium must involve a dual reaction of the substance whereat each of the tautomeric forms yields its own derivatives.

Pseudomerism concepts were developed by Ingold and Thorpe [82] in the twenties; at present they are shared by Hückel [83].

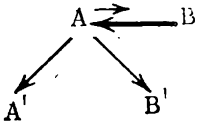
If the equilibrium $A \rightleftarrows B$ is displaced toward $A$ (equilibrium constant $K_T \ll 1$), then the formation of $A'$ from $A$ is quite probable. But the formation of $B'$ from $B$ under an equilibrium greatly displaced toward $A$ is not always possible, because the conversion of the equilibrium mixture $A \rightleftarrows B$ into $B'$ according to the mechanism of pseudomeric transformation

$$A \underset{k_2}{\overset{k_1}{\rightleftarrows}} B \xrightarrow{k_3} B' \,(K_T = K_1/K_2)$$

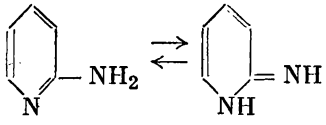
is always slower than the direct conversion $A \rightarrow B'$ at the same initial concentration. If $K_T$ is very small (less than $10^{-10}$) the rate of formation of $B'$ by the mechanism $B \rightarrow B'$ is very small (due to the low concentration of $B$). To make the formation of B' from $B$ take place at an observable rate, the reaction rate constant $K_3$

of $B \rightarrow B'$ must be enormously large (of the order of $10^{10}$-$10^{12}$ l/mol$^{-1}$ sec$^{-1}$ for monomolecular, and $10^{10}$-$10^{11}$ l/mol$^{-1}$ sec$^{-1}$ for bimolecular transformations). However, such high reaction rates are not characteristic of reactions between organic molecules, but may exist only in the case of ionic or radical (or atomic) reactions. Thus, it follows from the above discussion that in tautomeric equilibria $A \rightleftarrows B$ greatly displaced towards $A$ ($K_T \ll 10^{-10}$) $B'$ practically does not form from $B$ and, therefore, $B'$ forms directly from $A$. This means that the hypothesis of pseudomerism is not applicable to greatly displaced equilibria. But if the equilibrium $A \rightleftarrows B$ is not greatly displaced, it is an ordinary tautomeric equilibrium (the lower limit for $K_T$ is about $10^{-6}$-$10^{-8}$). In these cases the presence of the form $B$ can be proved and its concentration measured. Consequently, there is no place for the hypothesis of pseudomerism and this concept should be abandoned.

The dual reactive nature of tautomeric substances with a greatly displaced equilibrium is determined by the reaction taking the two possible routes without transfer of the reaction centre and with transfer of the reaction centre. Both series of derivatives arise from $A$ and not from $B$:

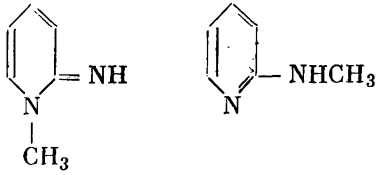



A large number of such reactions are known. Thus, the dual reactivity characteristic of α-aminopyridine was interpreted as a tautomeric phenomenon by Chichibabin:




(I) (II)

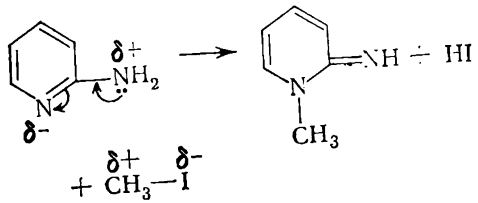
Methylation of aminopyridine with alkyl halides yields *N*-methylpyridonimine (III), and methylation of its sodium salt produces methylaminopyridine (IV):




(III) (IV)

Goldfarb and Setkina [85] showed, by investigating the absorption spectra of α-aminopyridine, that if form (II) is present in the mixture its quantity is so small that it cannot be identified spectrally.

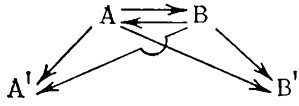
It follows from this that pyridonimine derivatives form from tautomer (I) and not (II), with transfer of the reaction centre:



Other examples of this kind may be given: the dual reactivity of aldoximes and ketoximes, of isatin, α- and γ-pyridones, α-hydroxyquinoline, amides of carboxylic acids and others.

In these cases, apparently, dual reactivity is not a consequence of tautomerism, although the substances are tautomeric. The tautomeric equilibrium is greatly displaced in the direction of one of the forms which is the one that gives both series of derivatives.

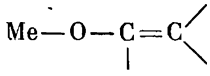
When the tautomeric equilibrium is not displaced strongly in one direction (such as in β-dicarbonyl compounds, nitroparaffins, nitrosophenols) both of the forms may react. However, as the reaction may proceed with or without transfer of the reaction centre, derivatives $B'$ may form from $B$ as well as from $A$ in the general case; and derivatives $A'$ may also arise from either $A$ or $B$, according to the scheme:



The actual form any particular derivative of a tautomeric substance stems from can be determined only as a result of a special investigation in each separate case.

### 10-2.4 Factors Determining Whether the Reaction Will or Will Not Involve Transfer of the Reaction Centre

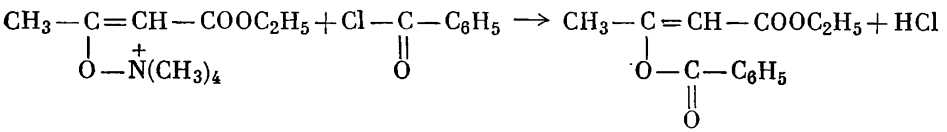
Factors determining whether a reaction will or will not involve transfer of the reaction centre have not been sufficiently studied. Only occasional observations and informal generalization have been made so far in this field. In the cases of dual reactivity of



enolates with the system in their molecules they may be summarized as follows [44]:

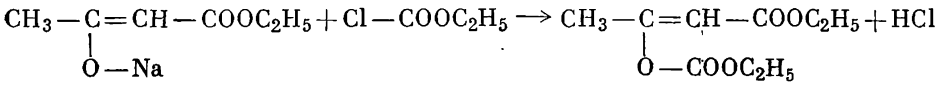
1. If the oxygen-metal bond is strongly ionized, and the reagent attacking the enolate is a cation or a strongly electrophilic molecule* then the fast reaction is the one at the oxygen.

For example, the tetramethylammonium enolate of acetoacetic ester is acylated by benzoyl chloride (in a mixture of alcohol and ether) exclusively at the oxygen while the sodium enolate of aceto-



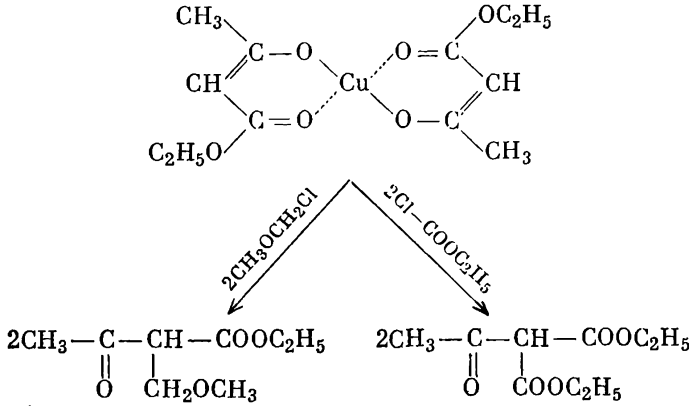
acetic ester (the bond between sodium and oxygen is less ionized) benzoylates in different solvents only at the carbon.

A stronger electrophilic reagent, chlorocarbonic ester, reacts at the oxygen even with sodium acetoacetate:



2. If the active reagent is strongly electrophilic, but the oxygen-metal bond in the enolate is not ionized or weakly ionized, the reaction at the oxygen goes slowly. The reaction at the carbon predominates with transfer of the reaction centre.

An example is the reaction of the copper acetoacetate with chloromethyl ether or with chlorocarbonic ester:



* The electrophilic properties of alkylating agents increase approximately in the following sequence:

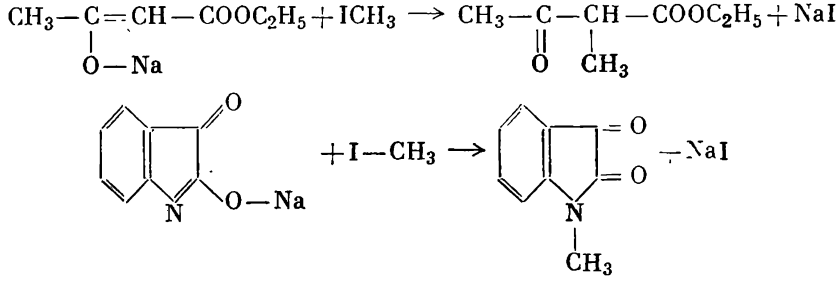
$$RI < R_2SO_4 < CH_2=CH-CH_2Cl < C_6H_5CH_2Br < CH_3OCH_2Cl < < (C_6H_5)_2CCl_2 < (C_6H_5)_3CCl < (O_2NC_6H_4)_3CBr$$

and those of acylating agents—in the sequence

$$R-COCl < Cl-COOC_2H_5$$

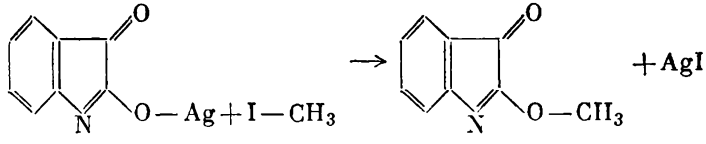
3. Predominance of the reaction at the carbon is also observed when the reagent is weakly electrophilic but the oxygen-metal bond is strongly ionized.

For example, alkyl halides react with sodium salts of keto-enols at the carbon and with sodium salts of lactim-lactams at the nitrogen:

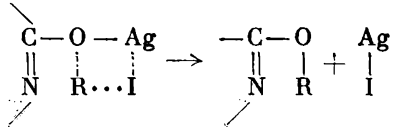


4. In the case of a weakly electrophilic reagent with an unionized oxygen-metal bond the reaction proceeds predominantly at the oxygen and the process is slow.

An example is the reaction between alkyl halides and silver salts of keto-enols and lactim-lactams, e.g.:



It is possible that in such cases the lower activation energy at the oxygen is also due to the occurrence of an additional reaction between the metal and the halogen:



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## APPENDIX

TABLE I **Heats of Formation of Organic Compounds from Atoms in Gas State at $T = 298.16°K$ (250°C)***

| Substance | Heat of formation, kcal |
|---|---|
| *Saturated hydrocarbons* | |
| Methane | −352.61±0.075 |
| Ethane | −585.49±0.116 |
| Propane | −820.62±0.142 |
| *n*-Butane | −1056.15±0.179 |
| 2-Methylpropane | −1057.79±0.164 |
| *n*-Pentane | −1291.88±0.16 |
| 2-Methylbutane | −1293.80±0.20 |
| 2,2-Dimethylpropane | −1296.55±0.25 |
| *n*-Hexane | −1527.38±0.19 |
| 2-Methylpentane | −1529.08±0.25 |
| 3-Methylpentane | −1528.44±0.23 |
| 2,2-Dimethylbutane | −1531.77±0.23 |
| 2,3-Dimethylbutane | −1529.91±0.24 |
| *n*-Heptane | −1762.85±0.19 |
| *n*-Octane | −1998.32±0.20 |
| *n*-Nonane | −2233.78±0.22 |
| *n*-Decane | −2469.25±0.26 |
| *n*-Dodecane | −2940.18±0.34 |
| *n*-Hexadecane | −3882.05±0.53 |
| *n*-Eicosane | −4823.91±0.74 |
| *Alkenes* | |
| Propene | −686.74±0.122 |
| Butene | −922.31±0.19 |
| *cis*-Butene-2 | −923.99±0.30 |
| *trans*-Butene-2 | −924.74±0.24 |
| 2-Methylpropene | −926.45±0.26 |
| *cis*-Pentene-2 | −1159.23±0.26 |
| *trans*-Pentene-2 | −1160.29±0.26 |
| 2-Methylbutene-1 | −1161.38±0.23 |
| 2-Methylbutene-2 | −1162.87±0.22 |
| 3-Methylbutene-1 | −1159.62±0.22 |

* Data from V. M. Tatevsky "Chemical Structure of Hydrocarbons and Regularities in Their Physico-Chemical Properties" (in Russian). Moscow University Press, 1953.

*(Continued)*

| Substance | Heat of formation, kcal |
|---|---|
| *cis*-Hexene-2 | −1394.80±0.53 |
| *trans*-Hexene-2 | −1395.80±0.53 |
| *cis*-Hexene-3 | −1394.80±0.53 |
| *trans*-Hexene-3 | −1395.80±0.53 |
| Pentene-1 | −1157.70±0.43 |
| Hexene-1 | −1393.20±0.44 |
| Octene-1 | −1864.14±0.45 |
| Nonene-1 | −2099.60±0.46 |
| Decene-1 | −2335.07±0.48 |
| *Dienes* | |
| Butadiene | −782.5 |
| *Acetylenic hydrocarbons* | |
| Acetylene | −388 |
| Propyne | −543.12±0.21 |
| Butyne-1 | −778.50±0.21 |
| Butyne-2 | −783.30±0.24 |
| Pentyne-1 | −1014.02±0.50 |
| Pentyne-2 | −1017.72±0.50 |
| Hexyne-1 | −1249.51 |
| Heptyne-1 | −1484.98 |
| Octyne-1 | −1720.44 |
| Nonyne-2 | −1955.91 |
| Decyne-1 | −2191.37 |
| *Alycyclic hydrocarbons* | |
| Cyclopentane | −1171.16 |
| Methylcyclopentane | −1409.04 |
| Ethylcyclopentane | −1644.15 |
| *n*-Propylcyclopentane | −1879.71 |
| *n*-Butylcyclopentane | −2115.08 |
| 1,1-Dimethylcyclopentane | −1646.83 |
| *cis*-1,2-Dimethylcyclopentane | −1644.74 |
| *trans*-1,2-Dimethylcyclopentane | −1646.45 |
| *cis*-1,3-Dimethylcyclopentane | −1645.71 |
| *trans*-1,3-Dimethylcyclopentane | −1646.25 |
| Cyclohexane | −1412.67±0.19 |
| Methylcyclohexane | −1650.77±0.25 |

*(Continued)*

| Substance | Heat of formation, kcal |
|---|---|
| Ethylcyclohexane | −1885.37±0.37 |
| *n*-Propylcyclohexane | −2121.06±0.30 |
| *n*-Butylcyclohexane | −2356.35±0.33 |
| 1,1-Dimethylcyclohexane | −1887.58±0.46 |
| *cis*-1,2-Dimethylcyclohexane | −1885.47±0.45 |
| *trans*-1,2-Dimethylcyclohexane | −1887.34±0.46 |
| *cis*-1,3-Dimethylcyclohexane | −1888.48±0.43 |
| *trans*-1,3-Dimethylcyclohexane | −1886.52±0.43 |
| *cis*-1,4-Dimethylcyclohexane | −1886.54±0.43 |
| *trans*-1,4-Dimethylcyclohexane | −1888.44±0.43 |
| *Aromatic and alkylated aromatic hydrocarbons* | |
| Benzene | −1050.89±0.12 |
| Toluene | −1289.30±0.15 |
| Ethylbenzene | −1524.67±0.20 |
| *o*-Xylene | −1527.25±0.26 |
| *m*-Xylene | −1527.67±0.18 |
| *p*-Xylene | −1527.50±0.24 |
| *n*-Propylbenzene | −1760.46±0.20 |
| Isopropylbenzene | −1761.39±0.26 |
| *n*-Butylbenzene | −1996.17±0.31 |
| *n*-Amylbenzene | −2231.64±0.37 |
| *n*-Hexylbenzene | −2467.10±0.39 |
| *n*-Heptylbenzene | −2702.57±0.42 |
| *n*-Octylbenzene | −2938.03±0.46 |
| *n*-Nonylbenzene | −3173.50±0.50 |
| *n*-Decylbenzene | −3408.97±0.54 |
| Naphthalene | −1644.57 |
| Anthracene | −2239.03 |
| Phenanthrene | −2250.19 |
| Chrysene | −2839.92 |
| Pyrene | −2490.10 |
| Perylene | −3076.75 |

TABLE II **Energies of Single and Multiple Bonds (in kcal/mole)* (Heat of Sublimation of Diamond is Taken as 124.3 kcal/mole)**

| Bond | Bond energy | Bond | Bond energy |
|---|---|---|---|
| | | *Single bonds* | |
| H—H | 103.4 | Si—Br | 69.3 |
| C—C | 58.6 | F—F | 63.5 |
| Si—Si | 42.5 | Cl—Cl | 57.8 |
| Ge—Ge | 42.5 | Br—Br | 46.1 |
| N—N | 20.0 | I—I | 36.2 |
| P—P | 18.9 | C—H | 87.3 |
| As—As | 15.1 | Si—H | 75.1 |
| O—O | 34.9 | N—H | 83.7 |
| S—S | 63.8 | P—H | 63.0 |
| Se—Se | 57.6 | As—H | 47.3 |
| O—H | 110.2 | Si—I | 51.1 |
| Si—H | 87.5 | Ge—Cl | 104.1 |
| Se—H | 73.0 | N—F | 68.8 |
| H—F | 147.5 | N—Cl | 38.4 |
| H—Cl | 102.7 | P—Cl | 62.8 |
| H—Br | 87.3 | P—Br | 49.2 |
| H—I | 71.4 | P—I | 35.2 |
| C—Si | 57.6 | As—Cl | 60.3 |
| C—N | 48.6 | As—Br | 48.0 |
| C—O | 70.0 | As—I | 33.1 |
| C—S | 54.5 | O—F | 58.6 |
| C—F | 107.0 | O—Cl | 49.3 |
| C—Cl | 66.5 | S—Cl | 66.1 |
| C—Br | 54.0 | S—Br | 57.2 |
| C—I | 45.5 | Se—Cl | 66.3 |
| Si—O | 89.3 | Cl—F | 86.4 |
| Si—S | 60.9 | Br—Cl | 52.7 |
| Si—F | 143.0 | I—Cl | 51.0 |
| Si—Cl | 85.8 | I—Br | 42.9 |
| | | *Multiple bonds* | |
| C=C | 100 | C=O (in $CH_2O$) | 142 |
| C≡C | 123 | | |

* After L. Pauling, "The Nature of the Chemical Bond", 2nd ed., Cornell University Press, Ithaca, N. Y., 1945.

*(Continued)*

| Bond | Bond energy | Bond | Bond energy |
|---|---|---|---|
| C=O (in other aldehydes) | 149 | C≡N (in other cyanides) | 150 |
| C=O (in ketones) | 152 | C=S | 103 |
| C=N | 94 | N≡N (as a base) | 170 |
| C≡N (in HCN) | 144 | | |

In compiling the above table the values given in Table 3 are taken as the heat contents of the gaseous atoms in the basic states (to which the bond energies are reduced), compared to the standard states (to which the heats of formation are reduced).

TABLE III **Heats of Formation of Elements from Monoatomic Gases Under Standard Conditions (in kcal/mole)***

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| H . . . 51.7 | Rb . . . 18.9 | Ge . . . . 85.0 | As . . 30.3 | F . . . 31.8 |
| Li . . . 39.0 | Cs . . . 18.8 | Sn . . . . 78.0 | O . . . 59.1 | Cl . . 28.9 |
| Na . . . 25.9 | C . . . . 124.3 | N . . . . 85.1 | S . . . 66.3 | Br . . 26.9 |
| K . . . 19.8 | Si . . . 85.0 | P . . . . 31.6 | Se . . 61.0 | I . . . 25.6 |

* After L. Pauling, "The Nature of the Chemical Bond", 2nd ed., Cornell University Press, Ithaca, N.Y., 1945.

TABLE IV **Atomic Refractions Calculated by Eisenlohr***

| Element | Atomic refraction | | | |
|---|---|---|---|---|
| | for D line of Na | for hydrogen lines | | |
| | | $H_\alpha$ | $H_\beta$ | $H_\gamma$ |
| Carbon | 2.418 | 2.413 | 2.438 | 2.466 |
| Hydrogen | 1.100 | 1.092 | 1.115 | 1.122 |
| Oxygen in carbonyl | 2.211 | 2.189 | 2.247 | 2.267 |
| Oxygen in ether | 1.643 | 1.639 | 1.649 | 1.662 |
| Oxygen in hydroxyl | 1.525 | 1.522 | 1.531 | 1.541 |
| Chlorine | 5.967 | 5.933 | 6.043 | 6.101 |
| Bromine | 8.865 | 8.803 | 8.999 | 9.152 |

* F. Eisenlohr. Spektrochemie organischer Verbindungen. Enke, Stuttgart, 1912.

*(Continued)*

| Element | Atomic refraction | | | |
|---|---|---|---|---|
| | for D line of Na | for hydrogen lines | | |
| | | $H_\alpha$ | $H_\beta$ | $H_\gamma$ |
| Iodine . . . . . | 13.900 | 13.757 | 14.224 | 14.521 |
| C=C (double bond) . . | 1.733 | 1.686 | 1.824 | 1.893 |
| C≡C (triple bond) . . | 2.398 | 2.328 | 2.506 | 2.538 |
| | (2.336) | | | |
| Nitrogen (prim. aliph.) | 2.322 | 2.309 | 2.368 | 2.397 |
| Nitrogen (sec. aliph.) | 2.499 | 2.475 | 2.561 | 2.603 |
| Nitrogen (tert. aliph.) | 2.840 | 2.807 | 2.940 | 3.00 |
| Nitrogen (nitrile) . . . | 3.118 | — | — | — |
| Nitrogen (imides) . . . | 3.776 | — | — | — |
| Fluorine . . . . . | 0.997 | — | — | — |
| Sulphur in RSH . . . . | 7.69 | — | — | — |

TABLE V **Values of Dipole Moments, Interatomic Distances and Differences in the Electronegativities of Atoms Forming the Bonds***

| Bond | Dipole moment, D | Interatomic distance, Å | Difference in electronegativity |
|---|---|---|---|
| C—H . . . . . | 0.4 | 1.07 | 0.4 |
| C—O . . . . . | 0.8 | 1.43 | 1.0 |
| C—N . . . . . | 0.45 | 1.47 | 0.5 |
| C—F . . . . . | 1.4 | 1.41 | 1.5 |
| C—Cl . . . . . | 1.5 | 1.76 | 0.5 |
| C—Br . . . . . | 1.4 | 1.91 | 0.3 |
| C—I . . . . . | 1.2 | 2.10 | 0.0 |
| N—H . . . . . | 1.31 | 1.00 | 0.9 |
| O—H . . . . . | 1.51 | 0.96 | 1.4 |
| S—H . . . . . | 0.68 | 1.34 | 0.4 |

* The internuclear distances given here are the sums corresponding to the Pauling covalent radii (L. Pauling, "The Nature of the Chemical Bond"). The differences in electronegativity were calculated also from Pauling's data (L. Pauling, *J. Amer. Chem. Soc.*, 54, 3570, 1932).

*(Continued)*

| Bond | Dipole moment, D | Interatomic distance, Å | Difference in electronegativity |
|---|---|---|---|
| H—Cl | 1.03 | 1.27 | 0.9 |
| H—Br | 0.78 | 1.41 | 0.7 |
| H—I | 0.38 | 1.61 | 0.4 |
| As—H | 0.10 | 1.51 | 0.1 |
| P—H | 0.36 | 1.40 | 0.0 |
| Cl—O | 0.73 | 1.65 | 0.5 |
| I—Br | 0.4 | 2.47 | 0.3 |
| P—Cl | 0.81 | 2.09 | 0.9 |
| P—Br | 0.36 | 2.24 | 0.7 |
| P—I | 0.0 | 2.43 | 0.4 |
| As—F | 2.03 | 1.85 | 2.0 |
| As—Cl | 1.64 | 2.20 | 1.0 |
| As—Br | 1.27 | 2.35 | 0.8 |
| As—I | 0.78 | 2.54 | 0.5 |
| Sb—Cl | 2.6 | 2.40 | 1.2 |
| Sb—Br | 1.9 | 2.55 | 1.0 |
| Sb—I | 0.8 | 2.74 | 0.7 |

TABLE VI **Dipole Moments of Some Aliphatic Compounds**

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution* | Gas |
| $CH_4$ | — | 0 |
| $CH_3—CH_3$ | — | 0 |
| $CH_3—OH$ | 1.66 | 1.69 |
| $CH_3—OCH_3$ | — | 1.29 |
| $CH_3—F$ | — | 1.81 |
| $CH_3—Cl$ | 1.86 | 1.83 |
| $CH_3—Br$ | 1.82 | 1.79 |
| $CH_3—I$ | 1.60 | 1.64 |
| $CH_3—CHO$ | — | 2.70 |
| $CH_3—CO—CH_3$ | 2.76 | 2.85 |

* Solution was generally in benzene.

*(Continued)*

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution* | Gas |
| $CH_3COOC_2H_5$ | 1.85 | 1.76 |
| $CH_3—CH$ | 3.44 | 3.94 |
| $CH_3—NH_2$ | — | 1.32 |
| $CH_3—N(CH_3)_2$ | — | 0.65 |
| $CH_3—NO_2$ | 3.02 | 3.54 |
| $C_2H_5—OH$ | 1.66 | 1.69 |
| *n*-$C_3H_7—OH$ | 1.71 | 1.64 |
| *n*-$C_4H_9—OH$ | 1.66 | 1.63 |
| *n*-$C_3H_7—Cl$ | 1.94 | 2.04 |
| *n*-$C_4H_9—Cl$ | 1.93 | 2.04 |
| *iso*-$C_3H_7Cl$ | 2.04 | 2.15 |
| *tert*-$C_4H_9Cl$ | — | 2.13 |
| $C_2H_5—Br$ | 1.88 | 2.01 |
| *n*-$C_3H_7—Br$ | 1.93 | 2.15 |
| *n*-$C_4H_9Br$ | 1.93 | 2.15 |
| *iso*-$C_3H_7Br$ | 2.04 | 2.19 |
| *tert*-$C_4H_9Br$ | 2.21 | — |
| $C_2H_5—I$ | 1.78 | 1.87 |
| *n*-$C_3H_7—I$ | 1.84 | 1.97 |
| *n*-$C_4H_9—I$ | 1.88 | 2.08 |
| *iso*-$C_3H_7—I$ | 1.84 | — |
| *tert*-$C_4H_9—I$ | 2.13 | — |
| $C_2H_5CHO$ | 2.54 | 2.73 |
| *n*-$C_3H_7CHO$ | 2.57 | 2.72 |
| *n*-$C_4H_9CHO$ | 2.57 | — |
| *iso*-$C_3H_7CHO$ | 2.56 | — |
| *iso*-$C_3H_7—OH$ | 1.70 | 1.68 |
| *tert*-$C_4H_9OH$ | 1.66 | — |
| $C_2H_5Cl$ | — | 2.00 |
| $C_2H_5CN$ | 3.57 | 4.03 |
| *n*-$C_3H_7CN$ | 3.57 | 4.05 |
| *n*-$C_4H_9CN$ | 3.57 | 4.09 |
| *iso*-$C_3H_7CN$ | 3.61 | — |
| *tert*-$C_4H_9CN$ | 3.65 | — |
| $C_2H_5—NH_2$ | 1.38 | — |
| *n*-$C_4H_9NH_2$ | 1.40 | — |
| *tert*-$C_4H_9NH_2$ | 1.29 | — |
| $C_2H_5—NO_2$ | 3.19 | 3.70 |

*(Continued)*

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution* | Gas |
| $n$-$C_3H_7$—$NO_2$ | — | 3.72 |
| $n$-$C_4H_9$—$NO_2$ | 3.29 | — |
| *iso*-$C_3H_7$—$NO_2$ | — | 3.37 |
| *tert*-$C_4H_9$—$NO_2$ | — | 3.71 |
| $CH_3$—$CH$=$CH_2$ | — | 0.35 |
| $CH_2$=$CH$—$CH_2$—$CH_3$ | — | 0.30 |
| $C_2H_5SH$ | — | 1.56 |
| $CH_2$—$CH_2$ | — | 1.88 |
| O | — | 1.88 |
| $CH_2OH$—$CH_2OH$ | — | 2.28 |
| $CH_2NH_2$—$CH_2NH_2$ | — | 1.94 |
| $CH_2OH$—$CH_2Cl$ | — | 1.88 |
| $CH_2$=$CH$—$Br$ | — | 1.41 |
| $CH_2$=$CH$—$I$ | — | 1.26 |
| $CH_2$=$CCl$—$CH$=$CH_2$ | — | 1.42 |
| $CH \equiv CH$ | — | 0 |
| $CH_3C \equiv CH$ | — | 0.75 |
| $C_2H_5C \equiv CH$ | — | 0.80 |
| $C_3H_7C \equiv CH$ | — | 0.85 |
| $C_4H_9C \equiv CH$ | — | 0.87 |
| $C_5H_{11}C \equiv CH$ | — | 0.86 |
| $CH_2$=$CHCl$ | — | 1.44 |
| $CH \equiv C$—$Cl$ | — | 0.44 |
| $CH \equiv C$—$Br$ | — | 0 |
| $C_4H_9C \equiv CCl$ | 1.23 | — |
| $C_4H_9C \equiv CBr$ | 1.06 | — |
| $C_4H_9C \equiv Cl$ | 0.75 | — |
| $C_5H_{11}C \equiv CCl$ | 1.27 | — |
| $C_6H_{11}C \equiv CBr$ | 1.05 | — |
| $C_5H_{11}C \equiv Cl$ | 0.80 | — |
| $(CH_3)_2C$=$CH_2$ | — | 0.49 |
| *trans*-$CH_3CH$=$CH$—$CH$=$CH_2$ | — | 0.68 |
| $CH_2$=$C(CH_3)$—$CH$=$CH_2$ | — | 0.38 |
| $CH_2$=$C(CH_3)$—$C(CH_3)$=$CH_2$ | — | 0.52 |
| $CH_2$=$CH$—$CHO$ | 2.88 | 3.04 |
| $CH_2$=$CH$—$CN$ | — | 3.88 |
| $CH_3CH$=$CH$—$CN$ | — | 4.50 |

*(Continued)*

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution* | Gas |
| $CH_3CH=CH-CHO$ | 3.67 | — |
| *trans*-$CH_3CH=CH-COOH$ | 4.50 | — |
| $CH_2=C=O$ | 1.43 | 1.45 |
| $(CH_3)_3NO$ | 5.02 | — |
| $(CH_3)_3N \cdot BF$ | 5.76 | — |
| $(CH_3)_3N \cdot BCl_3$ | 6.23 | — |
| $C_2H_5NH_2 \cdot AlCl_3$ | 6.94 | — |
| $(C_2H_5)_2O \cdot BF_3$ | 5.29 | — |
| $(C_2H_5)_2O \cdot BCl_3$ | 5.98 | — |
| $(C_2H_5)_2O \cdot AlCl_3$ | 6.68 | — |
| $(CH_3)_3P \cdot BCl_3$ | 7.03 | — |
| $(C_2H_5)_2S \cdot BCl_3$ | 6.00 | — |
| $CH_2Cl_2$ | — | 1.55 |
| $CH_2Br_2$ | — | 1.43 |
| $CH_2I_2$ | — | 1.08 |
| $CHF_3$ | — | 1.59 |
| $CHCl_3$ | — | 1.02 |
| $CHBr_3$ | — | 0,99 |
| $CHI_3$ | — | 0.80 |
| $CH_3CHCl_2$ | — | 2.07 |
| $CH_3CCl_2CH_3$ | — | 2.25 |
| $CH_3CCl_3$ | — | 1.78 |
| $CH_3CF_3$ | — | 2.27 |
| $C_2H_5NC$ | 3.47 | — |
| *iso*-$(C_4H_9)_2SO$ | 3.90 | — |
| $(CH_3)_2SO_2$ | — | 4.44 |
| $CO_2$ | — | 0 |
| $CO$ | — | 0.1 |
| $CS_2$ | — | 0 |
| $CCl_4$ | — | 0 |

TABLE VII **Dipole Moments of Some Aromatic and Heterocyclic Compounds**

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution | Gas |
| $C_6H_6$ | 0 | 0 |
| $C_6H_5CH_3$ | 0.41 | 0.37 |
| $C_6H_5—C_2CH_3$ | — | 0.6 |
| $C_6H_5F$ | 1.45 | 1.57 |
| $C_6H_5Cl$ | 1.56 | 1.73 |
| $C_6H_5Br$ | 1.53 | 1.71 |
| $C_6H_5I$ | 1.30 | — |
| $C_6H_5OH$ | 1.61 | 1.40 |
| $C_6H_5OCH_3$ | 1.16 | 1.35 |
| $C_6H_5CHO$ | 2.75 | — |
| $C_6H_5COCH_3$ | 2.93 | 3.00 |
| $C_6H_5COOC_2H_5$ | 1.92 | 1.95 |
| $C_6H_5CN$ | 3.90 | 4.37 |
| $C_6H_5NC$ | 3.5 | — |
| $C_6H_5NO_2$ | 3.97 | 4.24 |
| $C_6H_5NH_2$ | 1.52 | 1.48 |
| $o$-$C_6H_4(CH_3)_2$ | 0.55 | — |
| $m$-$C_6H_4(CH_3)_2$ | 0.4 | — |
| $p$-$C_6H_4(CH_3)_2$ | 0 | — |
| $p$-$C_6H_4(CH_2Cl)_2$ | 2.2 | — |
| $p$-$C_6H_4(COOCH_3)_2$ | 2.2 | — |
| $p$-$C_6H_4(CHO)_2$ | 2.35 | — |
| $p$-$C_6H_4(NH_2)_2$ | 1.5 | — |
| $p$-$C_6H_4[N(CH_3)_2]_2$ | 1.29 | — |
| $o$-$C_6H_4(OH)_2$ | 2.16 | — |
| $p$-$C_6H_4(NO_2)[N(CH_3)_2]$ | 6.87 | — |
| $p$-$C_6H_4(NO_2)(OC_2H_5)$ | 4.76 | — |
| $p$-$C_6H_4(NO_2)NH_2$ | 6.10 | — |
| $p$-$C_6H_4(NO_2)OH$ | 5.04 | — |
| $p$-$C_6H_4(NO_2)Br$ | 2.65 | — |
| $p$-$O_2NC_6H_4—N=\overset{+}{N}=\overset{-}{N}$ | 2.96 | — |
| $C_6H_5N(CH_3)_2$ | 1.58 | 1.61 |
| $C_6H_5—N=\overset{+}{N}=\overset{-}{N}$ | 1.55 | — |
| $C_6H_5CH_2Cl$ | 1.82 | — |
| $C_6H_5CCl_3$ | — | 2.07 |
| $o$-$C_6H_4(NO_2)_2$ | 6.00 | — |

*(Continued)*

| Compound | Dipole moment, D | |
|---|---|---|
| | Solution | Gas |
| $m$-$C_6H_4(NO_2)_2$ | 3.79 | — |
| $p$-$C_6H_4(NO_2)_2$ | 0 | — |
| $C_6H(CH_3)_4OH$* | 1.68 | — |
| $C_6H(CH_3)_4Br$* | 1.55 | — |
| $C_6H(CH_3)_4NO_2$* | 3.39 | — |
| $C_6H(CH_3)_4NH_2$* | 1.39 | — |
| $O_2NC_6(CH_3)_4N(CH_3)_2$* | 4.11 | — |
| $O_2NC_6(CH_3)_4OC_2H_5$* | 3.69 | — |
| $O_2NC_6(CH_3)_4NH_2$* | 4.98 | — |
| $O_2NC_6(CH_3)_4OH$* | 4.08 | — |
| $O_2NC_6(CH_3)_4Br$* | 2.36 | — |
| $C_6H_2(CH_3)_3NO_2$** | 3.64 | — |
| $C_6H_2(CH_3)_3N(CH_3)_2$** | 1.03 | — |
| $C_6H_2(CH_3)_3NH_2$** | 1.40 | — |
| $C_6H_2(CH_3)_3F$** | 1.36 | — |
| $C_6H_2(CH_3)_3Cl$** | 1.55 | — |
| $C_6H_2(CH_3)_3Br$** | 1.52 | — |
| $C_6H_2(CH_3)_3I$** | 1.42 | — |
| *Heterocyclic Compounds* | | |
| Pyridine | 2.25 | — |
| Quinoline | 2.19 | — |
| Dimethyl-γ-pyrone | 4.05 | — |

* Durene derivatives.
** Mesitylene derivatives.

TABLE VIII **Characteristic Frequencies* of Vibrations of Atomic Groups** in Infrared Spectra**

| Group | Frequency, $cm^{-1}$ | Wavelength, μ | Group | Frequency, $cm^{-1}$ | Wavelength, μ |
|---|---|---|---|---|---|
| C—C | 1000 | 10 | C—O | 1150 | 8.5 |
| C—N | 1100 | 9 | C—F | 1200 | 8.3 |

* Frequencies (in $cm^{-1}$) and wavelengths (in μ) are indicated approximately, because frequencies of vibrations of the same groups are different in different molecules. If the frequency value ends with two zeros, it means that it varies within ± 100 $cm^{-1}$ relative to the given value. If the frequency ends in one zero, the deviation may be ± 50 $cm^{-1}$ and if the last cipher is 5 the probable deviation is ± 10 to 20 $cm^{-1}$. Frequencies of OH and N—H may decrease in comparison with indicated values by 200 $cm^{-1}$, and the lines corresponding to them widen (to 200 $cm^{-1}$ and more) because of the presence of hydrogen bonds in liquid water and liquid ammonia.

** Foil A. Miller, "Application of Infrared and Ultraviolet Spectra to Organic Chemistry", In *Organic Chemistry* ed. by Gilman, Vol. III, Chap. 2, New York, 1953.

*(Continued)*

| Group | Frequency, cm$^{-1}$ | Wavelength, μ | Group | Frequency, cm$^{-1}$ | Wavelength, μ |
|---|---|---|---|---|---|
| C—S . . . . . | 650 | 15.4 | C=C (aromatic) | 1595 | 6.27 |
| C—Cl . . . . . | 750 | 13.3 | C=N . . . . . | 1640 | 6.10 |
| C—H (acetylenic) | 3350 | 3.0 | C=N (*iso*) . . . | 2150 | 4.65 |
| C—H (ethylenic) | 3020 | 3.30 | C=O (in anhydrides) . . . . . | 1775 | 5.63 |
| C—H (aromatic) | 3080 | 3.25 | | 1825 | 5.48 |
| C—H (aliphatic) | 2890 | 3.46 | C=O (in esters) | 1745 | 5.73 |
| N—H (amide and amine) . . . . | 3400 | 2.9 | C=O (in acids) | 1710 | 5.85 |
| N—H (imine) . . | 3375 | 2.95 | C=O (in ketones) . . . . | 1695 | 5.90 |
| O—H . . . . . | 3600 | 2.78 | C=S . . . . . | 1530 | 6.54 |
| Si—H . . . . . | 2260 | 4.42 | C≡C . . . . . | 2220 | 4.50 |
| P—H . . . . . | 2350 | 4.26 | C≡N . . . . . | 2250 | 4.45 |
| S—H . . . . . | 2585 | 3.87 | $CH_3$—(methyl) | 1385 | 7.22 |
| Se—H . . . . . | 2230 | 4.48 | C—O—C (ether) | 565 | 17.70 |
| H—F . . . . . | 3959 | 2.59 | | 985 | 10.15 |
| H—Cl . . . . . | 2886 | 3.46 | $C=CH_2$ . . . . | 1410 | 7.09 |
| H—Br . . . . . | 2559 | 3.91 | $CF_3$ . . . . . | 1380 | 7.25 |
| H—I . . . . . | 2231 | 4.48 | $-NO_2$ . . . . . | 1565 | 6.3 |
| C=C (ethylenic) | 1640 | 6.10 | | | |
| C=C (conjugated) | 1590 | 6.30 | | | |

TABLE IX **Values of Covalent Radii* and van der Waals Radii** of Elements**

| Element | Covalent radius Å | Van der Waals radius Å | Element | Covalent radius Å | Van der Waals radius Å |
|---|---|---|---|---|---|
| H . . . . | 0.30 | 1.17 | N= . . . | 0.60 | |
| B— . . . | 0.88 | | N≡ . . . | 0.547 | |
| B= . . . | 0.76 | | O— . . . | 0.66 | 1.38 |
| B≡ . . . | 0.68 | | O= . . . | 0.55 | |
| C— . . . | 0.771 | | F . . . . . | 0.64 | 1.35 |
| C= . . . | 0.665 | 1.8 | Si— . . . | 1.17 | |
| C≡ . . . | 0.602 | | Si= . . . | 1.07 | |
| N— . . . | 0.70 | 1.57 | Si≡ . . . | 1.00 | |

* L. Pauling, "The Nature of the Chemical Bond", 2nd ed., Cornell University Press, Ithaca, N.Y., 1945.

** N. V. Sedgwick, *Ann. Rep. Chem. Soc.*, **29**, 64 (1933); S. B. Hendricks, *Chem. Rev.*, 7, 427 (1933); L. Pauling, ibid., 189.

*(Continued)*

| Element | Covalent radius Å | Van der Waals radius Å | Element | Covalent radius Å | Van der Waals radius Å |
|---|---|---|---|---|---|
| P— . . . | 1.10 | 1.19 | Se— . . . | 1.17 | 2.00 |
| P= . . . | 1.00 | | Se= . . . | 1.07 | |
| P≡ . . . | 0.93 | | Br . . . . | 1.14 | 1.95 |
| S— . . . | 0.04 | 1.85 | Sn— . . . | 1.40 | |
| S= . . . | 0.94 | | Sn= . . . | 1.30 | |
| Cl . . . | 0.99 | 1.80 | Sb— . . . | 1.41 | |
| Ge— . . . | 1.22 | | Sb= . . . | 1.31 | |
| Ge= . . . | 1.12 | | Te— . . . | 1.37 | |
| As— . . . | 1.21 | 2.0 | Te= . . . | 1.27 | |
| As= . . . | 1.11 | | I . . . . . | 1.33 | 2.10 |

TABLE X **Experimentally Determined Ordinary Bond Lengths (Interatomic Distances)**

| Bond | Bond length in Å | Compound | Bond | Bond length in Å | Compound |
|---|---|---|---|---|---|
| C—C | 1.54* | Saturated aliphatic compounds | C—N | 1.42 | Pyrrole |
| | | | C—N | 1.37 | $CO(NH_2)_2$ |
| C—C | 1.57 | $CH_3CH_3$ | C—N | 1.15 | $CN_3—CN$ |
| C—C | 1.47* | $CH_2=CH—CH=CH_2$ | C—F | 1.42* | $CH_3F$ |
| C—C | 1.462 ± | $CH_3—C\equiv CH$ and | C—F | 1.32 | $CH_2F_2$ |
| | ± 0.005* | $CH_3—C\equiv C—CH_3$ | C—F | 1.33 | $CHF_3$ |
| C—H | 1.09 | $CH_4$ | C—F | 1.38* | $C_6H_5F$ |
| C—H | 1.06 | $HC\equiv CH$ | C—Cl | 1.77* | $CH_3Cl$ |
| C—O | 1.44 | $CH_3O—CH_3$ | C—Cl | 1.77* | $CH_2Cl_2$ |
| C—O | 1.46 | Dioxane | C—Cl | 1.77* | $CHCl_3$ |
| C—O | 1.27 | H—COONa | C—Cl | 1.76 | $CCl_3CHO$ |
| C—O | 1.31 | $CaCO_3$ | C—Cl | 1.69* | $CH_2=CHCl$ |
| C—S | 1.82 | $CH_3—S—CH_3$ | C—Cl | 1.69* | $C_6H_5Cl$ |
| C—S | 1.74 | Thiophene | C—Cl | 1.82* | $CH\equiv C—CH_2—Cl$ |
| C—N | 1.47 | $N(CH_3)_3$ | C—Cl | 1.80* | $CH_2=CHCH_2—Cl$** |
| C—N | 1.46* | $CH_3—NO_2$ | C—Cl | 1.82* | $CH_3COCl$** |

* Electronographically obtained values.

** P. A. Akishin, L. V. Vilkov, R. M. Tatevsky, *Vestn. Moskovsk. Universit*, No. 1, 143 (1957).

*(Continued)*

| Bond | Bond length in Å | Compound | Bond | Bond length in Å | Compound |
|---|---|---|---|---|---|
| C—Br | 1.91 | Saturated aliphatic bromides | N—O | 1.41 | $HONO_2$ |
| | | | O—O | 1.48 | $H_2O_2$ |
| C—Br | 1.95* | $CH \equiv C—CH_2—Br$ | O—O | 1.26 | $O_3$ |
| C—Br | 1.80* | $CH \equiv C—Br$ | O—H | 0.97 | $H_2O$ |
| C—Br | 1.79 | $N \equiv C—Br$ | S—H | 1.35 | $H_2S$ |
| C—I | 2.12 | Saturated aliphatic iodides | F—H | 0.92 | HF |
| | | | Cl—H | 1.27 | HCl |
| N—N | 1.48 | $H_2N—NH_2$ | Br—H | 1.42 | HBr |
| N—H | 1.01 | $NH_3$ | I—H | 1.60 | HI |
| N—O | 1.37 | $H_2NOCH_3$ | | | |

TABLE XI **Experimentally Determined Multiple Bond Lengths (Interatomic Distances)**

| Bond | Bond length in Å | Compounds | Bond | Bond length in Å | Compounds |
|---|---|---|---|---|---|
| C=C | 1.34 | $CH_2=CH_2$ | C=N | 1.18 | $\overset{1}{C}H_3—\overset{2}{N}=\overset{3}{C}$ |
| C=C | 1.33* | $C_6H_5CH=CHC_6H_5$ | | (2,3) | |
| C=C | 1.32 | Benzoquinone | C=N | 1.34* | $CH_2=\overset{+}{N}=\overset{-}{N}$ |
| C≡C | 1.20* | $CH \equiv CH$, | C=N | 1.36 | Pyridine |
| | | $CH \equiv C—C \equiv CH$ | C≡N | 1.16* | $(CN)_2$ |
| | | $CH \equiv CX$, | C≡N | 1.15 | $CH_3—CN$ |
| | | $Br—C \equiv CBr$ | N=O | 1.11 | Cl—N=O |
| C=O | 1.21* | $CH_2O$ | | 1.14 | Br—N=O |
| C=O | 1.20* | $CH_3CHO$ | $\overset{+}{N}—\overset{-}{O}$ | 1.36* | $(CH_3)_3\overset{+}{N}—\overset{-}{O}$ |
| C=O | 1.13 | CO | (*iso*-N=O) | | |
| C=O | 1.163 | $CO_2$ | | | |
| C=O | 1.31 | $Ca^{++}CO_3^{--}$ | | | |
| C=S | 1.45* | $CS_2$ | Ditto | 1.21 | $Na^+\left[O=N\begin{matrix}O\\O\end{matrix}\right]$ |
| C=S | 1.56 | COS | | | |
| C—N | 1.44 (1,2) | | Ditto | 1.22 | $CH_3—N\begin{matrix}O\\O\end{matrix}$ |

* Electronographically determined values.

TABLE XII **Atomic and Structural Parachore* Values**

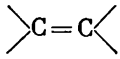
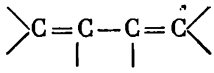
| | | | |
|---|---|---|---|
| Carbon | 4.8 | Double bond | 23.2 |
| Hydrogen | 17.1 | Triple bond | 46.6 |
| Nitrogen | 12.5 | Three-membered ring | 16.7 |
| Phosphorus | 37.7 | Four-membered ring | 11.6 |
| Oxygen | 20.0 | Five-membered ring | 8.5 |
| Sulphur | 48.2 | Six-membered ring | 6.1 |
| Fluorine | 25.7 | Esters | 3.2 |
| Chlorine | 54.3 | Semipolar bond | 1.6 |
| Bromine | 68.0 | Single-electron bond | 11.6 |
| Iodine | 91.0 | | |

* S. Sugden. *J. Chem. Soc.*, 1177 (1924).

TABLE XIII **Atomic Susceptibilities and Increments of Some Simple Bonds***

| | $\chi_A \times 10^6$ |
|---|---|
| Hydrogen | −2.93 |
| Carbon | −6.00 |
| Nitrogen | |
| in chains | −5.57 |
| in rings | −4.61 |
| in monoamides | −1.54 |
| in diamides and imides | −2.11 |
| Oxygen | −4.61 |
| combined with an atom of carbon | +1.73 |
| in a carboxyl group | −3.36 |
| Fluorine | −11.5 |
| Chlorine | −20.1 |
| Bromine | −30.6 |
| Iodine | −45 |
| Sulphur | −15.0 |
| Phosphorus | −26.3 |

*(Continued)*

| | $\lambda \times 10^6$ | | $\lambda \times 10^6$ |
|---|---|---|---|
|  | +5.5 | $C_{III}$** | −4.0 |
|  | +10.6 | | +3.1 |
| $CH_2=CH-CH_2-$ | +4.5 | | +4.1 |
| $-N=N-$ | +1.8 | | +4.1 |
| $-N=O$ | +1.7 | | +1.4 |
| $C_{tert}$ | −1.29 | | |
| $C_{quat}$ | −1.54 | | |
| $C_I$** | −0.24 | | |
| $C_{II}$** | −3.1 | | |

* V. Klemm, "Magnetochemistry", Part III.

** CI corresponds to the position of a carbon atom in an aromatic compound belonging to one ring; $C_{II}$ and $C_{III}$ to atoms belonging simultaneously to two or three rings, respectively.

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